Exhibit A

UNITED STATES DISTRICT COURT
DISTRICT OF NEW JERSEY

MDL No. 2789
Honorable Claire C. Cecchi

IN RE: PROTON-PUMP INHIBITOR PRODUCTS LIABILITY LITIGATION (NO. II)

THIS DOCUMENT RELATES TO:
Civil Action No.: 2:17-cv-06124

FREDDY BALES,
Plaintiff
VS
ASTRAZENECA PHARMACEUTICALS LP, et al.,
Defendants

Civil Action No.: 2:17-cv-02475

DAVID FOSTER,
Plaintiff
VS
ASTRAZENECA PHARMACEUTICALS LP, et al.,
Defendants

Civil Action No.: 2:18-cv-03159

STEVE KERSCH,
Plaintiff
VS
ASTRAZENECA PHARMACEUTICALS LP, et al.,
Defendants

Civil Action No.: 2:17-cv-00212

KIMBERLY LEE,
Plaintiff
VS
ASTRAZENECA PHARMACEUTICALS LP, et al.,
Defendants

CONFIDENTIAL - PURSUANT TO PROTECTIVE ORDER

GILBERT W. MOECKEL, M.D., PH.D., FASN

July 7, 2021

Civil Action No.: 2:17-cv-13727

DIANE NELSON,
Plaintiff

VS

ASTRAZENECA PHARMACEUTICALS LP, et al.,
Defendants

Civil Action No.: 2:19-cv-00850

JAMES RIEDER,
Plaintiff

VS

ASTRAZENECA PHARMACEUTICALS LP, et al.,
Defendants

Videotaped deposition of
GILBERT W. MOECKEL, M.D., PH.D., FASN
taken via Zoom videoconference before Clifford Edwards, Certified Shorthand Reporter and Notary Public, on July 7, 2021, at 11:19 a.m.

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LEO RAKITIN, ESQ., ASTRAZENECA
JEFF FLEMING, VIDEOGRAPHER/EXHIBIT TECHNICIAN

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(continued)

THE VIDEOGRAPHER: We are now on the record. My name is Jeff Fleming. I'm a videographer for Golkow Litigation Services. Today's date is July 7, 2021. The time is 11:19 a.m.

This remote video deposition is being held in the matter of Proton-Pump Inhibitor Products Liability Litigation, in the United States District Court, District of New Jersey.

The deponent is Dr. Gilbert Moeckel.

All parties to this deposition are appearing remotely and have agreed to the witness being sworn in remotely. Due to the nature of remote reporting, please pause briefly before speaking to ensure all parties are heard completely.

All appearances will be noted on the stenographic record.

The court reporter is Cliff Edwards and will now swear in -- swear in the witness.

GILBERT W. MOECKEL, M.D., PH.D., FASN, doing business at 310 Ceder Street New Haven, Connecticut, having first been duly sworn, deposed and testified as follows:

DIRECT EXAMINATION

BY MS. ALTHOFF:

Q Good morning, Dr. Moeckel. My name is Katherine Althoff. I am here in this litigation representing AstraZeneca. I think before we got started, you're also aware that Mr. James Mizgala is on. He is here representing Takeda. And we are here to take your deposition starting this morning and probably continuing into tomorrow.

Are you aware of that?

A Yes.

Q And, Dr. Moeckel, the address that you gave to the court reporter just a moment ago, what type of address was that?

A That is my work address.

Q And where are you today, sir?

A I am in a conference room of the Department of Pathology at Yale School of Medicine.

Q And what is the address there, Dr. Moeckel?

A The address is 310 Cedar Street in New Haven, Connecticut.

Q And who is in the room with you today, Dr. Moeckel?

A In the room is Paul Pennock and Bess DeVaughn.

Q And these are, to your understanding, attorneys representing plaintiffs in this litigation?

A Yes.

Q And as I understand it, you've been retained as an expert witness on behalf of plaintiffs in this litigation; correct?

A Yes.

Q And that's what we're here to talk to you about today?

A Yes.

Q And, Doctor, as you can imagine, I'm not there in the room with you, nor is Mr. Mizgala. We are on Zoom today due to the -- what is the continuing effects of the pandemic. So the rules are a little bit different than it would be if we were all in the same room in the

sense that I would ask that you not communicate verbally or nonverbally with any of the lawyers in the room, staff or others sort of off camera, if you will, other than during breaks.

Do you understand that?

A Yes.

Q And the same applies with regard to any electronic devices you have. You agree that you won't receive any text messages or other information during this deposition that would relate to your testimony; okay?

A Yes.

Q And I saw from your report, Dr. Moeckel, that you've been deposed before. So you've been through this sort of proceeding before; correct?

A Yes.

Q Is this the first one where some or all the lawyers have been via Zoom or some other electronic platform?

A Yes.

Q Same rules apply as, you know, if we were all in person together. The only difference I would say, Doctor, is if you can make sure that you let me finish my question before you start

answering, and I will try to do the same for you with regard to your answer, so that we don't cut one another off on Zoom, which is even more important than it would be in a normal deposition; okay?

A Yes.

Q Doctor, did you receive the notice of deposition or subpoena for deposition for your deposition today?

A I -- I did not receive a written notice of the subpoena, no.

MS. ALTHOFF: Jeff, let's show him our number one and have it marked as Exhibit 1.

(Whereupon, Exhibit No. 1, Defendants' Notice of Oral Videotaped Deposition and Associated Subpoena Duces Tecum of Gilbert W. Moeckel, M.D., PH.D., FASN, was marked for identification.)

BY MS. ALTHOFF:

Q So, correct, Dr. Moeckel, you've not seen this document before today?

A Well, I --

MS. ALTHOFF: Scroll down a couple pages here.

THE WITNESS: Okay. Is there a way you can make this a little bit larger, please, if possible?

MS. ALTHOFF: Uh-huh.

THE WITNESS: Oh, yeah. That's much better.

BY MS. ALTHOFF:

Q Again, the question for you, Dr. Moeckel, is: Have you seen this document before today?

A No, I have not.

MS. ALTHOFF: If we could go to the Exhibit A to this document, please.

BY MS. ALTHOFF:

Q And, Doctor, this Exhibit A asks you to bring some documents with you, including your current curriculum vitae, any bills, invoices, etc., that you've prepared, as well as some other information.

Did you bring anything with you today?

A I brought a copy of my expert report with appendices pertaining to study material and my CV.

Q When you say appendices relating to the study materials, can you describe that for me a little bit more with particularity?

A Yeah. Those are lists of the study names that I reviewed.

Q Is that a document that you prepared, sir?

A It was prepared for me.

Q Have you or anyone on your behalf, to your knowledge, Dr. Moeckel, prepared a document which would reflect the amount of time and/or charges that you have spent as it relates to this litigation?

A Yes.

The attorney's office prepared a statement of compensation, I believe it's called, that includes the payments made for my work as a expert witness.

Q And I know that we're going to be getting a copy of that later today, but I guess my question for you is: Do you have a sense, Dr. Moeckel, as you sit here today, of how much you have charged so far?

A I believe it's a little over $120,000.

Q Uh-huh.

And based on the information that we received as a part of your report, that was -- is that based on $400 an hour for consultation and report review?

A Yes, that is correct. $400 per hour.

Q And do I understand that you're getting paid $500 an hour for your testimony today?

A Yes, that is true.

MR. PENNOCK: Objection. Note my objection.

BY MS. ALTHOFF:

Q And would that be the same charge, $500 an hour, should you testify at trial?

A Yes.

Q The approximately a hundred twenty thousand that you identified as how much so far -- well, let me ask this question: The hundred and -- approximately hundred and twenty thousand, is that monies that have been paid already or is that sort of the value of the work that you've done so far?

A That is money that has been paid already.

Q And do you have additional charged time before today that you've not yet been paid for?

A Yes.

Q And how much value do you have that you haven't been paid yet?

A Approximately, $12,000.

Q Uh-huh.

And the hundred and twenty thousand that you've identified, was that up through the time that your report was prepared?

A It was up through the time the report was prepared, but also includes time I spent preparing for this deposition.

Q So the additional 12,000 that you've not yet been paid for, what does that relate to?

A That does relate to the time I spent on the deposition today and tomorrow and also additional preparation that I have not billed yet.

Q Additional preparation for this deposition?

A Yes.

Q Dr. Moeckel, you've been retained by the plaintiffs; correct?

A Yes.

Q And when were you first retained?

A I believe in 2018, if I remember correctly.

Q Do you know approximately when in 2018 you were retained by the plaintiffs?

A I would say sometime spring, early summer.

Q And I think, according to your report, is it fair that you were retained to review animal data from various manufacturers?

A Yes, that's true.

Q Setting aside that sort of general scope of work, were there other scope of work that you were asked to -- to do as part of your expert work in this litigation?

A No. I don't remember anything beyond the --

Q So for instance, were you -- have you been asked to render any opinions about human renal pathology?

A I believe I was shown a couple of kidney biopsy reports at some point.

Q And have you -- and, I -- I guess, maybe I -- I don't have my realtime in front of me.

So the kidney biopsies that you saw, they were of humans?

A They were reports -- only reports of

human kidney biopsies, yes.

Q Okay. And you've not rendered any opinions that you intend to testify in this case with regard to those two biopsies --

A No.

Q -- that you reviewed; correct?

A Correct, yeah.

Q Do you -- and you don't intend to enter any opinions at all in this litigation with regard to the causes of any kidney disease in any particular patient whose case is presented at trial in this matter?

A That's right.

Q Other than having reviewed some biopsy -- human biopsy reports and reviewed animal data from the various manufacturers, any other sort of scope of work that you've taken on as it relates to this litigation?

A No. I do not remember any other work except for I have just mentioned.

Q In your report, Dr. Moeckel, you identified two cases in which you had testified in the last four years; is that correct?

A You mean basically depositions that I have been part of?

Yes.

Q Well, have -- have you testified in any depositions or at trial in the last four years?

A Yes, I have.

Q And was it only two or are there more?

A No. Just two depositions.

Q So you identified the Dominguez plaintiff, Diana Dominguez (phonetic) case, and the plaintiff Patricia McGilliard (phonetic) case.

So those are the two where you've testified?

A Yes, that is correct.

Q And the Diana Dominguez vs. Raghu Juvvadi (phonetic) case, who did you testify on behalf of -- well, let me ask this question instead.

Did you serve as an expert witness in either one of those cases?

A Yes. I served as expert witness in both of these cases.

Q So in the Diana Dominguez vs. Raghu Juvvadi case, who -- upon -- for which party did you testify?

A For the defendant.

Q Uh-huh. And in the Patricia McGilliard

vs. Kaye Zuckerman, M.D., et al., case, did you testify as an expert witness on behalf of Mrs. Gilliard [sic] or one of the defendants?

A I -- I believe I was a expert witness for the plaintiff in that case.

Q And in your day-to-day practice, Dr. Moeckel, you are a renal pathologist; correct?

A Yes.

Q And you spend the majority of your time on human renal pathology; correct?

A Yes.

Q And so were you testifying in one or both of those cases as a renal pathology -- human renal pathology expert?

A Yes. In the case -- the first case that you mentioned, the one that was in a court in Florida, I believe, there I was a expert witness as renal pathologist.

Q And what about in the Patricia McGilliard vs. Kaye Zuckerman case that was in the Superior Court of New Haven, presumably Connecticut?

A Right.

There I was the attending on an autopsy report and was questioned regarding the

circumstances of the patient's death as the attending who performed the autopsy on that patient.

Q So in the second case, although you may have had expert-type opinions, you were also a fact witness?

A Yes.

Q Did either one of those cases involve proton-pump inhibitors in any way?

A No.

Q Did either of these patients, Diana Dominguez or Patricia McGilliard, have any form of interstitial nephritis that you were asked to review?

A No.

Q Did either of these patients have chronic kidney disease?

A Yes.

So the first case, the one in Florida, was a case of a kidney biopsy report that stated IGA nephropathy, which is a chronic kidney disease.

And I was -- and I was asked to comment on the report, its accuracy, and how it should be interpreted.

Q So Ms. Dominguez had chronic kidney disease which had been attributed to IGA nephropathy?
A Yes.
Q And as part of her care and treatment, she had a biopsy?
A Yes.
Q And you were asked to confirm whether the biopsy, in fact, showed IGA nephropathy?
A Yes.
Q And were you able to determine on biopsy that, in fact, it did show IGA nephropathy as the cause of her chronic kidney disease?
A No. In my opinion from the biopsy, it could not be concluded that the diagnosis was IGA nephropathy.
Q And were you able to determine on that biopsy what the cause of Ms. Dominguez's chronic kidney disease was?
A No.
Q Have you ever testified, Dr. Moeckel, as a animal renal pathologist?
A No.
Q Have you ever testified, Dr. Moeckel, whether in the last four years or otherwise, about

the relationship between animal histopathology and human disease?

A No.

Q So fair to say the types of opinions that are reflected in your expert report in the proton-pump inhibitor litigation, this is the first time you've expressed those types of opinions as an expert witness in litigation?

A Yes. That's correct.

Q Dr. Moeckel, what did you do to prepare for your deposition?

A I reviewed my report. I reviewed scientific applications. And I reviewed some of the studies that I think were, you know, important and featured in my report.

Q Okay. Did you meet with any lawyers?

A Yes, I did.

Q And who did you meet with?

A Paul Pennock and Bess DeVaughn.

Q And how many times did you meet with Mr. Pennock?

A Four or -- four or five times, predominantly via Zoom.

Q How much total time did you spend with Mr. Pennock?

A Four hours.

Q And Attorney DeVaughn, how much -- was -- was she in the same meetings or were these different meetings?

A She was in the same meetings.

Q Did you have any separate meetings with Ms. DeVaughn?

A I think I had one or two Zoom meetings just with her.

Q And how much additional time did you spend with her?

A Two hours.

Q So approximately six hours total meeting with lawyers?

A Yes.

Q You said you reviewed your report. I'm assuming the report that you've entered in this litigation; correct?

A Yes.

Q And you said you reviewed some scientific publications?

A Yes.

Q Did you review any scientific publications, other than what is referenced, you know, by citation in your report -- your

AstraZeneca report?

A No.

Q And you said you reviewed studies that figured, you know, more prominently in your report.

And I just want to make sure. By that, are you talking about the actual animal data from the manufacturers?

A Yeah. I'm talking about the studies that are featured in the report and the material that I had access to.

Q Right.

And I -- I just want to make sure. We're -- when you say "studies," we're talking about the internal nonclinical study reports and data?

A Yes.

Q Did you review any of those internal nonclinical, preclinical studies other than the ones that are listed in either Appendix A, Appendix B, or the body of your report?

A No.

Q Other than reviewing your report, reviewing some of the scientific publications that are cited in your report, reviewing some of the

studies that figure more prominently in your report and meeting with lawyers, was there anything else that you did to prepare for your deposition?

A No.

Q Have you spoken, in preparation or at any time, with any of the plaintiffs in this litigation?

A No.

Q Did you review any plaintiffs' depositions?

A Can you repeat that question, please?

Q Sure.

Did you review the depositions of any plaintiffs?

A No.

Q Did -- you mentioned that you had been asked to look at some kidney biopsy reports. But other than that, have you been asked to review or have you reviewed any medical records of any plaintiffs in this litigation?

A No.

Q What is your understanding with regard to the medical conditions that the plaintiffs in this litigation are complaining about?

A Can you repeat -- please repeat the question?

Q Sure.

What is your understanding of the medical conditions that the plaintiffs are complaining about in this litigation?

A I have the understanding that the plaintiffs complain about chronic kidney disease as a consequence of proton-pump inhibitor use.

Q Any other medical conditions that is your understanding that plaintiffs in this case are complaining about as a result of use of PPIs?

A No. I think that was all that I understood.

Q Have you spoken with any of the plaintiffs' healthcare providers?

A No.

Q Have you read any healthcare provider depositions?

A No.

Q And I think we talked about this previously, but I want to make sure I -- I got this right.

So you're not here today to testify that PPIs were the cause of any particular

injuries or claims by any particular plaintiff in this litigation?

A Yes, that's right.

Q Have you spoken with any of your colleagues or other medical professionals about your opinions in this case?

A No.

Q Have you reviewed any expert reports from any other expert for the plaintiffs?

A No.

Q Have you reviewed any expert reports from any defense expert?

A I believe I have seen the expert report by Dr. Sandusky (phonetic).

Is that the right pronunciation?

Q Uh-huh.

A I -- I have seen that expert witness report.

Q And you said you've -- you've seen it. I mean, you've -- you've read it; correct?

A Yes. I read it. Yes.

Q And did anything in Dr. Sandusky's report change or modify in any way your opinions that you're here to testify about today?

A No.

Q And other than Dr. Sandusky's report, have you reviewed any other defense expert reports?

A No.

Q Have you reviewed Dr. Martin Smith's report?

A I believe I have seen the report, but I have not read it in depth.

Q Okay. Did you read or review sections of that report?

A I read sections of that report, I believe, yes.

Q And did you review that report before you wrote your -- you know, signed off on your report or after?

A After.

Q And which sections of Dr. Smith's report do you recall reviewing?

A I recall reviewing the initial part where he talks about the chemical properties of PPIs and the toxicity and general discussion of toxicity mechanisms of drugs in the kidney.

Q Did you review Dr. Smith's analysis of the internal company animal or preclinical data?

A No.

Q Have you had any conversations with Dr. Smith at any time about this litigation?
A No.
Q Have you had any discussions with any other expert on behalf of the plaintiff about this case?
A No. No.
Q Have you reviewed Dr. John Danziger's report?
A No.
Q Have you reviewed the reports of any epidemiologist or biostatistician?
A No.
Q Have you reviewed the expert report of Dr. Colvin?
A Yes, I did.
Q And do you understand that Dr. Robert Colvin has been retained by the defense?
A Yes.
Q Okay. Do you know Dr. Colvin?
A Yes.
Q And how do you know him?
A He's a colleague of mine. He's a renal pathologist.
Q Uh-huh.

Do you have any criticisms of his reputation or credentials?

A No. He's an excellent renal pathologist.

Q Did you have any dispute with the opinions set forth in Dr. Colvin's report?

A No. I thought that the -- his expert witness report was very general.

Q Uh-huh.

A So I did not have anything specific that I objected.

Q And, of course, Dr. Colvin's report is on human renal pathology as opposed to animal pathology; correct?

A I believe that's what I remember, yes.

Q Did you have any -- sorry. Going back to Dr. Sandusky's report for a minute.

Did you have any criticisms of Dr. Sandusky's report?

A If I --

MR. PENNOCK: Just note my objection. I mean, this is all by memory.

So go ahead.

THE WITNESS: Yeah.

A As far as I remember, Dr. Sandusky in his report says that the lesions that were seen in the animal studies are all chronic progressive nephropathy. And I disagree with that opinion.

BY MS. ALTHOFF:

Q You understand, Dr. Moeckel, that the studies that were reviewed were both dogs and rodents; correct?

A Yes.

Q And dogs don't generally have lesions described as chronic progressive nephropathy; correct?

A That's right.

Q And so are you saying that Dr. Sandusky described lesions in dogs as chronic progressive nephropathy?

A I think that's what I remember.

Q And you said you disagreed that all the lesions that were seen were chronic progressive nephropathy.

Do you agree that all the lesions that were seen in the rodents, that being mice and rats, were chronic progressive nephropathy?

A I disagree that they are chronic progressive nephropathy.

Q Okay. Well, we'll be talking about that some more later.

Have you reviewed any of the reports from any nephrologist retained by either the plaintiffs or the defendants?

A No, I have not.

Q So you've not reviewed Dr. Cheriton (phonetic), Dr. Sirota (phonetic)?

A No. No, I have not reviewed their reports.

Q Okay. Now that we've gone through and -- and you do recall having reviewed Dr. Colvin's report and Dr. Sandusky's report and portions of Dr. Smith's report.

Are there any other expert reports that, as you sit here today, you can recall having reviewed?

A I do not recall reading any other report than those you just mentioned.

Q Uh-huh.

Have you reviewed any transcripts from any depositions in this case?

A No, I have not.

Q All right. Let's talk about your qualifications as set forth in your report in your

CV; okay?

A Okay.

Q Does not appear to me that you are a veterinarian or veterinary pathologist.

Is that correct?

A I'm not a veterinary pathologist, no.

Q And do you have training and expertise in toxicology?

A I have training in toxicology as pertaining to a full medical school training.

I also trained in residency in anatomic and clinical pathology, and part of the training as a pathology resident is to learn about toxicology and some toxicology procedures and tests and what mechanism underlie toxicological mechanisms.

Q Do you consider yourself a toxicologist?

A No, I do not.

Q As I understand it from looking at your report, you're not rendering any opinions regarding the manner in which the studies were actually conducted; is that correct?

A That is correct.

Q Instead, your opinions relate to how

the studies were interpreted or whether additional studies should have been done based on the findings that you saw in the studies?

A Yes. That is correct.

Q As a renal pathologist, are you a nephrologist?

A No. I am not a nephrologist.

Q And presumably, not a gastroenterologist either; correct?

A No.

Q Do you prescribe medications to patients?

A No, I do not.

Q Other than reviewing renal biopsies, do you treat kidney disease?

A No, I do not treat the disease.

Q Do you consider reading renal biopsies to be care and treatment of patients with renal disease?

A Yes, I do.

Q And in fact, on a day-to-day basis, you review tissue samples from patients who have chronic kidney disease; correct?

A Yes. And much more than that. I always review the clinical history, the other

laboratory findings, because interpreting a kidney biopsy is a part of a overall gestalt analysis of the patient.

I always review the serum creatinine values. I always -- always review BUN values. I look at the urinalysis results. I look at what the -- their clinical history is, what other diseases the patient have that might not be nephrological, pertaining to nephrology.

So I always look at the patient in its entirety.

Q So you have a good understanding then, Dr. Moeckel, of what kidney disease looks like in U.S. patients; correct?

A Yes, I do.

Q And that would include everything from acute interstitial nephritis, to acute kidney injury, to chronic kidney disease; is that right?

A Yes, that's right.

Q And you would have a good understanding of what underlying comorbidities, for example, are strongly correlated with chronic kidney disease?

A Yes, I do.

Q And as part of that understanding, you're well aware that hypertension and diabetes

are overwhelmingly the leading causes of chronic kidney diseases; correct?

MR. PENNOCK: Objection to form.

Go ahead.

A Yes, I understand.

BY MS. ALTHOFF:

Q With regard to acute interstitial nephritis -- which you've diagnosed before on biopsy; correct?

A Yes.

Q And when you've diagnosed it on biopsy, have you also received various clinical information from the clinicians about that patient?

A Yes, I have.

Q And as part of that, you're aware that acute interstitial nephritis is accompanied by an acute drop in kidney function; correct?

A Yes. Usually it is associated with a drop in kidney function.

Q And AIN is thought to be an immune hypersensitivity reaction; right?

A Not always. It depends. Certain drugs induce a so-called hypersensitivity reaction, but then there are several other mechanisms that can

lead to an acute interstitial nephritis.

Q And would that include things like autoimmune diseases and infections?

A It could be exacerbated by an autoimmune disease, but there are -- in addition to hypersensitivity reaction, which is a certain immune mechanism, there are other molecular mechanisms that can cause an acute interstitial nephritis.

Q Would you agree, Dr. Moeckel, that hundreds of medications have been associated with acute interstitial nephritis?

MR. PENNOCK: Note my --

A Yes.

MR. PENNOCK: Note my objection to this line of questioning that has no bearing on the opinions offered in his report.

Go ahead.

I'll object as you go.

BY MS. ALTHOFF:

Q Would you also agree, Dr. Moeckel, that although acute interstitial nephritis is sometimes diagnosed on a clinical picture only, in order to have a definitive diagnosis there must be a

biopsy?

MR. PENNOCK: Again, objection. Beyond the scope of the opinions being offered by this expert.

Go ahead.

A Yes. A kidney biopsy is very helpful in diagnosing acute interstitial nephritis.

BY MS. ALTHOFF:

Q And would you agree, Dr. Moeckel, that on biopsy, although you can diagnose AIN, you can't necessarily tell what caused it?

A Sometimes --

MR. PENNOCK: Objection.

A Sometimes you can tell what caused it. The hypersensitivity reaction caused by drugs is -- shows a specific pattern that, with near certainty, allows you to say that this is very likely a drug that is the culprit.

BY MS. ALTHOFF:

Q However, Dr. Moeckel, would you agree that you can't tell what drug caused that hypersensitivity reaction leading to acute interstitial nephritis?

MR. PENNOCK: Objection. Form.

A So you can have an idea about a certain

group of drugs that caused hypersensitivity reaction because they are very well known to do that. There are other drugs that cause acute interstitial nephritis without hypersensitivity reaction. And when they are on board, they become the likely culprit.

So you can from the biopsy get an idea what kind of drug category you are probably dealing with.

BY MS. ALTHOFF:

Q So in the category of drugs that cause hypersensitivity-reaction type of AIN, can you tell what drug caused the acute interstitial nephritis from the biopsy?

A Yeah. For instance, if a penicillin is given to the patient and you see a hypersensitivity reaction, then, more likely than not, the penicillin was the culprit causing the acute interstitial nephritis.

Q Yeah.

My question, Dr. Moeckel, is: If you don't know what drugs the patient has taken, but you see what appears to be a hypersensitivity reaction-type acute interstitial nephritis, can you tell from looking at the biopsy what drugs or

drug the patient took that caused it?

A If you don't know the medical list that the patient is on, you cannot conclude from the biopsy which drug caused the interstitial nephritis.

Q Going back to sort of your curriculum vitae, Dr. Moeckel, I looked through your list of editorial boards and professional organizations.

Is it correct that you don't serve on any editorial boards in journals of toxicology?

A That is correct.

Q And you don't belong to any professional societies of toxicology?

A Correct.

Q So for instance, you don't belong to the Society of Toxicologic Pathology?

A That's true.

Q Nor do you belong to the Society of Toxicology?

A That is true.

Q And you haven't published any articles in their journals; is that correct?

A As far as I remember -- and I don't remember every paper in my CV, but as far as I remember, I have not published in their journals.

Q Do you belong to any animal pathology working groups?

A No, I don't think so.

Q With regard to your publications, Dr. Moeckel, to the extent you've published on drug effects in animals, would you agree that all of those studies were short-term or acute studies?

A As far as I remember, they were predominantly studies that were running for a period less than one year, for sure.

Q Have you published at all, Dr. Moeckel, on the subject of chronic progressive nephropathy in rodents?

A No, I have not.

Q In your reference list, as well as in the materials considered list for your report, I saw that you had received or reviewed publications from, for instance, Dr. Seely.

Is that correct?

A Yes.

Q Would you agree that Dr. Seely is a well-respected and credentialed pathologist?

A Can you repeat the question?

Q Yeah.

Would you agree that Dr. Seely is a

credentialed and well-respected pathologist?

A If you pertain to human pathologist, I would say no. If you pertain to animal pathologist, I would say probably.

I am not a animal pathologist. I am not in a animal pathology society. So I cannot speak to the qualifications of Dr. Seely pertaining to animal pathology.

Q Thank you for that clarification. Yes, I meant animal pathology. So thank you for that.

You also cite Dr. -- some publications by Dr. Frazier; correct?

A Correct. Yes. Uh-huh.

Q And is Dr. Frazier a well-respected and credentialed animal pathologist?

A I don't know. I -- I am not aware -- I don't know him personally, and I -- I don't -- I'm not aware whether he is a, you know, well-accomplished animal pathologist, you know.

Q Last question like that: Dr. Gordon Hard, looks like you cited several publications from Dr. Hard as well; correct?

A Yes.

Q And do you know Dr. Hard?

A No. I do not know Dr. Hard.

Q Do you even know if Dr. Hard is alive?
A I don't know whether he is alive.
Q And is Dr. Hard a well-credentialed and respected animal pathologist?
A Again, I don't know.
Q Okay. Going back to your curriculum vitae, is it correct you've never worked on a pharmaceutical company?
A Say it again, slowly, please.
Q I'm sorry.
Is it correct that you've never worked at a pharmaceutical company?
A That is correct.
Q Have you designed any animal toxicity studies for drug approval that would be submitted to the FDA?
A No.
Q Have you ever been asked by a pharmaceutical company to review any of their toxicology studies before they would be submitted for drug approval to the FDA?
A No.
Q Have you ever been the primary animal study pathologist or a peer-review pathologist on any toxicology studies that were to be submitted

for FDA drug approval?

A No.

Q Have you ever worked at the FDA?

A No.

Q Have you ever served as a consultant or on any advisory committees to the FDA?

A Can you repeat that question?

Q Sure.

Have you ever served as a consultant to the FDA or served on an advisory committee to the FDA?

A No.

Q Have you ever had any communications with the FDA about proton-pump inhibitors?

A No.

Q All right. Let's talk about your case report that you've identified in your expert report; okay?

A Yes.

Q And the first author's last name is Ni; correct?

A Yes.

Q Was she a student of yours?

A She was a resident, I believe -- I believe, in medicine or surgery.

Q Uh-huh.

MS. ALTHOFF: And let's -- we can go ahead and pull it up. That might be helpful.

This is my 27. We'll mark it as Exhibit 2.

(Whereupon, Exhibit No. 2, "Late-Onset Omeprazole-Associated Acute Interstitial Nephritis," was marked for identification.)

BY MS. ALTHOFF:

Q Showing you what's been marked as Exhibit 2.

Dr. Moeckel, is this the case report that you and Ms. Ni submitted?

A Can you enlarge the image, please?

Q Sure.

And if we scroll down a little bit --

A Yes. Please. Go ahead.

Q -- we can see, I think, that -- your name and Nina Ni.

Do you see that?

A Yes.

Q And if we scroll back to the top, the title of this case report is "Late-Onset

Omeprazole-Associated Acute Interstitial Nephritis"; correct?

A That's correct, yes.

Q And this was submitted as a letter to the editor to the JAGS journal published in December of 2010.

Do you see that?

A Yes.

Q And do you know what journal that is, JAGS?

MR. PENNOCK: You -- you can ask to see --

THE WITNESS: Can I --

MR. PENNOCK: -- or pieces of this article --

THE WITNESS: Yeah. Can -- can --

MS. ALTHOFF: Oh, sure.

THE WITNESS: -- you show me the --

(Whereupon, the court reporter requests clarification.)

MS. ALTHOFF: I think he was asking you to scroll down.

BY MS. ALTHOFF:

Q Doctor, would you like him to continue

to scroll?

A Yes, please.

Q And this is the second page. If you want to continue to scroll down.

A Uh-huh.

Q Are you able to tell from reviewing this or do you recall what journal JAGS is, Dr. Moeckel?

A I do not recall.

Q Is this a nephrology journal?

A I believe it is, but I am not certain.

Q All right.

MS. ALTHOFF: Let's go up to the -- back up to the top of the first page, please, Jeff.

BY MS. ALTHOFF:

Q All right. I had a few questions I wanted to ask you about this case report, Doctor. So this --

MR. PENNOCK: I'm -- I'm sorry. Can I --

MS. ALTHOFF: Sure.

MR. PENNOCK: So is -- is this -- you marked this as an exhibit. I'm wondering why it hasn't been put in the

chat, or has it? Has it been put in the chat so that it can -- so that he can review it?

THE VIDEOGRAPHER: Yes, sir. It's in the chat.

MR. PENNOCK: It is? Okay. So if you go down, and then you can open it up yourself and have access to it.

THE WITNESS: Okay.

MS. ALTHOFF: Yeah. That's -- that's helpful, Paul -- thank you, 'cause the screen is only showing so much -- if he wants it blown up.

MR. PENNOCK: Well, he -- he's trying to open it right now.

MS. ALTHOFF: Doctor, just let us know when you've been able to open it up.

MR. PENNOCK: It's coming open now. There we go.

THE WITNESS: Uh-huh.

MS. ALTHOFF: Are we good?

THE WITNESS: Yes.

MS. ALTHOFF: Okay.

THE VIDEOGRAPHER: Doctor, if you

can, though, adjust -- if you can see it without adjusting the screen so I can see you better.

THE WITNESS: Is that better?

THE VIDEOGRAPHER: A little bit more, if you can, and you can still see the document, that would help, like -- that's great. Thank you.

BY MS. ALTHOFF:

Q All right. Doctor, my question is: Was your case report of a 73-year-old female who presented to the ER with an acute drop in kidney function?

A Can you repeat the question, please?

Q Sure.

This case report that you made, was it of a 73-year-old female who presented to the ER with an acute drop in kidney function?

A Yes.

Q With regard to her drop in kidney function, it was able to be detected by her primary care physician as well as the emergency department; correct?

A That is possible.

Q If you look at the second sentence of

your letter to the editor, Dr. Moeckel, it says, "Her primary care physician sent her" -- to the ER, presumably -- "after laboratory results revealed a serum creatinine of 2.9 mg/dL (baseline 0.7 mg/dL) and a high erythrocyte sedimentation rate."

Do you see that?

A Yes.

Q So her primary care physician was able to detect that this patient had a significant drop in her kidney function as reflected in her serum creatinine; correct?

A Correct.

Q By the time she got to the ER, this patient's serum creatinine had dropped -- or excuse me -- had risen additionally and now was at 3.5, if you look at the next paragraph; correct?

A Correct.

Q Going from a 0.7 serum creatinine to 2.9 and then 3.5, is that a significant drop in kidney function?

A Yes.

Q It notes in this report that you made, Dr. Moeckel, that this patient's BUN was 42 at the ER; is that correct?

A That's correct.
Q Normal is 10 to 20. So this was elevated; correct?
A Yes.
Q It also notes that she had white blood cells in her urine, which was described by you as sterile pyuria; correct?
A Correct.
Q And what does sterile pyuria indicate to a physician?
A That there are polymorph nuclear leukocytes in the urine.
(Whereupon, the court reporter requests clarification.)
A That there are polymorph nuclear leukocytes in the urine.
BY MS. ALTHOFF:
Q Can sterile pyuria or white blood cells in the urine also be a known side effect of taking acetaminophen?
A Can you repeat the question one more time, please?
Q Sure.
Are the detection of white blood cells in the urine a known side effect of taking

acetaminophen?

A Not that I know of.

Q It was noted in your case report that this patient had an elevated ESR and CRP.

Are those signs of acute interstitial nephritis, potentially?

A Let me review this.

Q Uh-huh.

A Can you repeat your question?

Q Sure.

If you look at the paragraph that starts with, "She was afebrile on physical examination, and her examination was unremarkable."

Do you see that paragraph?

A Yes.

Q Does it also state that her -- about halfway down -- her ESR was 104 millimeters per hour and her C-reactive protein was 43.9-milligrams per deciliter?

A Yes. It does say that, yes.

Q And are those quite elevated measurements?

A Yes, they are.

Q And is an elevated ESR and CRP a sign

of AIN, potentially?

A It can be seen with AIN.

Q Did this patient also report malaise, myalgia, weakness, and other nonspecific symptoms?

A So apparently the patient three to four weeks ago had malaise and headache and abdominal pain and myalgia.

Q And those were symptoms that she had reported to her primary care physician?

A That's what that seems to say, yes.

Q Uh-huh.

And are those symptoms that can be associated with acute interstitial nephritis?

A Yes.

Q Was it also the case that this 73-year-old female patient was taking several medications, including levothyroxine, omeprazole, and acetaminophen with caffeine?

A Yes, that's what the article says.

Q Uh-huh.

And with regard to the acetaminophen with caffeine -- acetaminophen is Tylenol; right?

A I believe so, yes.

Q Is it reflected in this report when the patient last took acetaminophen prior to admission

to the ER?

A Can you repeat the question?

Q Yeah. In fact, that wasn't a great question. Let me repeat that -- rephrase that question.

With regard to the acetaminophen and caffeine, it says she took it for occasional headaches.

Do you see that?

It's at the end of, I think, the first paragraph.

A Uh-huh.

Yes, that's true.

Q Do you know or did you have an understanding at the time you wrote this case report of when the last time this patient had taken acetaminophen with or without caffeine for headaches?

A I do not remember when was the last time she had taken acetaminophen with caffeine.

Q In the case report it reflects, with regard to her hospital course, that during her stay omeprazole was not given; is that correct?

If you want, we can scroll down, and I could show you where that is.

A Yeah. Why don't you do that.

Q Yeah. Okay. Come on here.

So it's at the bottom of the first paragraph -- or excuse me -- the bottom of the first column. It says, "Within the first 24 hours of presentation to the emergency department."

Do you see that?

A Yes.

Q And then on the second sentence, it says, "She was not given omeprazole during her hospital stay."

Do you see that?

A Yes.

Q And in this case report, it doesn't reflect whether the patient was given Tylenol or acetaminophen; correct?

A Do you mean during the hospital stay?

Q Yes, sir.

A Yeah. Let me quickly just continue reading.

Yeah. It was -- in this article, it does not say whether the acetaminophen and caffeine were continued during the hospital stay.

Q Are you aware of whether there are case reports, Dr. Moeckel, of acetaminophen temporally

associated with acute interstitial nephritis?

A As far as I know, acetaminophen is not a drug that is well known to cause acute interstitial nephritis.

Q Are there case reports, Dr. Moeckel, of acetaminophen temporally associated with acute interstitial nephritis?

A I assume there may be case reports. I have not read them recently.

Q Regardless of whatever the cause was of this patient's acute interstitial nephritis, you reported that she -- her serum creatinine levels continued to improve during her hospital stay and were at 1.9 milligrams per deciliter on discharge; correct?

A Correct.

Q And did you or Ms. Ni follow this patient following her discharge from the hospital?

A I believe that Ms. Ni may -- did follow the patient. I -- I believe so.

Q Does this case report reflect any post-discharge clinical course of the patient as it relates to her serum creatinine levels?

A Could you repeat your question?

Q Sure.

This clinical -- or this case report that you submitted, in terms of the clinical course of the patient, that information ends at discharge; correct?

A So it says her -- at hospital day five, the creatinine declined to 2.1.

Q And right above that, it says her serum creatinine continued to improve, and it gives what it was at admission, and then to 1.9 on discharge.

Do you see that?

A I -- I --

Q Right above the "By hospital Day 5."

A Yes. Yes. I see that, yes.

Q And my question to you, Dr. Moeckel, was: There's no information about what happened to this patient after she was discharged; correct?

MR. PENNOCK: Objection. You mean in -- in the -- in the published letter to the editor?

MS. ALTHOFF: Yes.

A Yeah. In -- in this article, we did not include information after her discharge, I believe.

BY MS. ALTHOFF:

Q All right. Let's move to your expert

report.

MR. PENNOCK: There's an idea.

MS. ALTHOFF: And, Jeff, it's my 2. Let's mark it as Exhibit 3.

(Whereupon, Exhibit No. 3, Proton Pump Inhibitor Toxicity Expert Witness Report, was marked for identification.)

BY MS. ALTHOFF:

Q Do you recognize, Dr. Moeckel, the first page of this report -- or this document as being your report?

A Yes, I do.

Could you please enlarge it?

Q Yes.

MR. PENNOCK: It's about --

BY MS. ALTHOFF:

Q And --

MR. PENNOCK: It's a little over an hour, but could we take a very quick break before we move into this?

MS. ALTHOFF: Yeah. Let me have him identify the exhibit, and then we'll take a break.

MR. PENNOCK: Great.

BY MS. ALTHOFF:

Q Let's go to page 28.

Dr. Moeckel, is that your signature on page 28?

A Yes. Yes, it is.

Q And did you sign this report on April 22nd of 2021?

A Yes, I did.

Q Okay. And is this the report that reflects the opinions -- all the opinions that you intend to offer at trial in this case?

A Yes.

Q Do you have any current plans to supplement this report?

A Well, I -- you know, I want to have the right to supplement in case additional information becomes available that would be pertinent to this expert witness report.

Q Yeah. Fair enough.

I -- I guess what I'm asking you is: As you sit here today, do you have any current plan to supplement this report with currently available information?

A No.

Q And any of the additional materials

that you have reviewed since you signed the report as we talked about -- you'd reviewed several expert reports, for instance -- did any of that information change or cause you to want to modify what's been marked here as Exhibit 3?

A No.

Q Okay. Thank you.

MS. ALTHOFF: Let's take a break. How long do you want to take, Paul?

MR. PENNOCK: Just five minutes, just to get up and --

MS. ALTHOFF: Okay.

THE VIDEOGRAPHER: Off the record 12:27 p.m.

(Whereupon, there was a recess taken from 12:27 p.m. to 12:38 p.m.)

THE VIDEOGRAPHER: On the record 12:38 p.m.

MS. ALTHOFF: Ah, there we go.

BY MS. ALTHOFF:

Q Dr. Moeckel, before we jump back into your report, just one follow-up question on the case report that we've been -- we're talking about with the 73-year-old female patient.

Correct that you determined that omeprazole-associated AIN was the diagnosis in this case?

A Sorry. Can you repeat the question again?

Q Yeah.

A There were some acoustic --

Q Oh, no problem. And -- and thank you for raising that, Dr. Moeckel. If anytime you can't hear or understand my question, please do ask me to restate it or rephrase it or repeat it, and I will.

So in this case, again, the 73-year-old female who presented to the ER with the acute drop in kidney function, in terms of this case report, you reported it as omeprazole-associated acute interstitial nephritis; correct?

A Yes.

Q Okay. And how did you determine that it was the omeprazole versus the levothyroxine or the Tylenol or something else?

A The main reason was that the omeprazole was the drug that was taken for a long period of time prior to the presentation in the ER, and the medication for headache was only taken on occasion

when the patient had headaches.

So I would say that -- and -- and our conclusion in this paper was that the proton-pump inhibitor was the only drug possible that could have caused this.

Q And, Doctor, was your conclusion affected in any way by the fact that when omeprazole was withheld in the hospital, her serum creatinine quickly improved?

A I don't remember. You know, this case report was more than ten years ago. I do not remember whether that was a -- a reason why we concluded.

However, in nephrology, if you discontinue a drug and the patient gets better, that is another piece of the evidence that that drug caused, likely, the lesion.

Q And, you know, we were talking earlier about acute interstitial nephritis being associated with drugs; correct?

A Yes.

Q And you had mentioned that some are due to hypersensitivity and some are other biologic processes; yes?

A Yes.

Q With regard to PPIs, would you agree that they've been classified as -- associated with acute interstitial nephritis as a hypersensitivity reaction?

MR. PENNOCK: Objection. No foundation. Objection to form.

Go ahead.

A I don't believe that that is true for every case. So that is something that I think is more the question to a nephrologist.

BY MS. ALTHOFF:

Q So you don't have an opinion one way or another, Dr. Moeckel, with regard to whether PPIs induce AIN potentially through a hypersensitivity reaction or through a different biologic process?

MR. PENNOCK: Again, note my objection. Beyond the scope of the report and the opinions offered in there, either report.

Go ahead.

A I believe that PPIs can cause an acute interstitial nephritis. I also believe that the mechanism is still enigmatic.

And I cannot, from the review of the literature, say with a hundred percent certainty

it is either one mechanism or the other. I think there's more research needed to understand the molecular mechanism of PPI-induced AIN.

BY MS. ALTHOFF:

Q Okay. Let's go back to your report, which has been marked as Exhibit 3.

Oh, there it is. Sorry. It took me a second.

Let's turn to page 3 of your report. And do you see the section entitled "Overview of Kidney"?

A Yes, I do.

Q Okay. And if you look at the last sentence on page 3, it says, "Acute drug-induced kidney injury may present as a clinically 'silent'" -- that in quotes -- "'injury' because blood clinical chemistry markers of renal function, such as serum creatinine and blood urea nitrogen, are unable to detect focal early stages of underlying tubular damage."

Is that what it says?

A Yes. I -- I can see that sentence and --

Q Dr. Moeckel, are you aware of any published case reports of PPI-induced kidney

injury that is clinically silent?

A I have not reviewed recently the case reports of PPI in respect to clinical silent or not and, therefore, I do not feel at this time point competent to answer this question.

Q Okay. Dr. Moeckel, in your practice, do clinicians typically do biopsies on patients who don't have a -- or who have a clinically silent kidney disease?

MR. PENNOCK: Objection.

Go ahead.

A I think it depends on the circumstance. If there are reasons to believe that a kidney tissue injury is present, although the creatinine does not show a significant increase at that time point, a biopsy might still be done.

For instance, the urinalysis may show features that point towards a kidney disease and triggers a biopsy even though the renal function may still be normal.

BY MS. ALTHOFF:

Q And so when you used the term then "clinically silent," you're only talking about changes in blood chemistries?

MR. PENNOCK: Objection.

A So clinically -- clinically silence means that there is no overt significant impairment in renal function. There might be other parameters in the many laboratory tests that we evaluate that might still be compelling to support a kidney biopsy.

So in other words, these physicians are very case-to-case dependent on the overall aspect of the patient and all additional information that comes into the patient evaluation. It's never something that is based only on, you know, one lab result.

BY MS. ALTHOFF:

Q And turning to page 4, which is, I think, where we are on the screen, of your report, you have a section where you discuss the differences and/or similarities between mammalian kidneys, that being rodents, dogs, humans, etc.; correct?

A Yeah. Can you show me where that is?

Q It's here on the screen, Dr. Moeckel.

A Uh-huh.

Q Do you see where it says, "Non-human mammalian kidneys (e.g., rodents, dogs, etc.) share similar anatomical and physiological

features with humans"?

A Yes.

Q Okay. Would you agree that animal -- or rats -- excuse me -- rats' and humans' kidneys are not completely the same?

A I think I would like to modify my answer to your question.

Anatomically, there are certainly differences between the rat and the human kidney. However, the histological structure of the -- of the functional unit is very, very similar between the human and the rat kidney.

So in other words, the nephron in the human kidney is very similar to the nephron in the rat kidney.

Q So pathologically, Dr. Moeckel, would you agree that humans' and rats' kidneys are not the same?

A I cannot agree to this question categorically, no. I would rather say that in many aspects, the rat and the human kidney are very similar.

Q Okay. Do humans develop calcium crystals at the corticomedullary junction?

A Can you repeat again? There was an

acoustic breakup.

Q Sure.

Do humans develop calcium crystals at the corticomedullary junction?

A They can develop these crystals at the corticomedullary junction, yes.

Q With regard to incidence, is it much higher in rats or humans?

A It depends whether you look at the normal kidney or whether you look under pathological conditions. I would say in the normal kidney, I would not expect to see crystals at the corticomedullary junction in either human nor a rat kidney.

Under certain pathological conditions, these crystals become much more common --

Q Is it --

A -- in both.

Q I'm sorry.

Is it a common toxicologic finding in rats to develop calcium crystals at the corticomedullary junction?

A To my knowledge, I am not aware that this is a common toxicological finding.

Q With regard to the urine of rats versus

humans, which one has higher osmolality?

A In regard to rats and humans, which one has the higher osmolality? Is this your question?

Q Yes.

A The rat has the higher osmolality, normally.

Q By a factor of what?

A I would say by a factor of three to five.

Q In whether -- in the rats versus humans, which one has higher urine protein content?

A The urine protein content is very much dependent on the nutrition. I don't think that you can categorically say, you know, one or the other.

Q Do rats have any specific proteins in their urine that humans do not?

A I'm not aware of a protein that the rat specifically excretes that the human does not excrete. However, the protein profiles may be different. That would not be surprising between different mammalian species.

Q Are you familiar with alpha-2 globulin in rats?

A Say it again.
Q Are you familiar with alpha-2 globulin in rats?
A I -- I have heard about this protein, yes.
Q And is it found in the protein -- or excuse me -- in the urine of all rats?
A I do not know.
Q Is it gender-specific in rats?
A I do not know.
Q When a rat experiences chronic nephritis, does its kidneys get larger or smaller?
A Depends on how far along the chronic disease -- the chronic kidney disease the rat is and the examination of the kidney is. So in late stages of chronic kidney disease, the kidney will be smaller because the kidney scars. That is also the fact in humans.
So at the very late stage of CKD, kidneys due to scarring usually get smaller.
Q And when you're reviewing -- referring to chronic kidney disease, are you using that synonymously with chronic nephritis?
A No. Chronic nephritis, as the term implies, is a chronic inflammatory condition of

the kidney.

Q Uh-huh.

A CKD, chronic kidney disease, can be caused by many other etiologies, such as hypertension, diabetes.

So I prefer the term "chronic nephropathy," because it encompasses all the several etiologic mechanisms that can lead to chronic kidney disease.

Q When a rat gets chronic nephropathy, does its kidneys get larger or smaller?

A Again, it depends at which time point you look. When you look late in chronic nephropathy, the kidneys should be small due to scarring.

Q And when a human has chronic nephropathy, does its kidneys get larger or shrink?

A Again, at the end of or the late phase of chronic kidney disease, the kidney will be smaller due to scarring.

Q Are you aware of whether humans experience alpha-2 globulin nephropathy?

A I have not personally experienced this disease in any of my patients, nor have I heard

this disease being discussed among any of my colleagues.

Q Would you agree it's generally accepted that the rat is not a good predictor of human toxicology for immune-mediated drug injuries to the kidneys?

A I disagree with that statement. I think that the rat is an excellent model to examine drug-mediated toxicity and other diseases that lead to chronic kidney disease.

And I have conducted animal experiments for the last 30 years. I have looked at hundreds and hundreds and hundreds of rat kidneys and mouse kidneys. I'm very familiar with rat and mouse kidneys in a wide variety of injury models, whether it is the ischemia-reperfusion, the 5/6 nephrectomy, the puromycin chronic glomerulosclerosis, the calcium phosphate nephropathy. Those are just a few of the models that I have worked with.

And so I feel very confident that I can evaluate any kind of mouse or rat kidney section in regards to a pathological lesion.

Q And specifically my question, Dr. Moeckel, was with regard to immune-mediated

drug injury?

A I --

MR. PENNOCK: Objection.

Could you restate the question, please?

MS. ALTHOFF: Sure.

BY MS. ALTHOFF:

Q Would you agree it's generally accepted that the rat is not a good predictor of human toxicology for immune-mediated drug injury to the kidneys?

A I do not think that the rat is a bad model to -- to examine immune-mediated drug toxicity. I think that the rat would be a possible model to investigate immune-mediated drug toxicity.

Q Are you familiar with Haschek and Rousseaux's Handbook of Toxicological Pathology?

A I am.

Q Is that a publication that is a -- a learned treatise on toxicologic pathology?

A It is a well-recognized textbook in the field.

Q Uh-huh.

MS. ALTHOFF: Let's pull up my 29.

I think we're on -- what? Exhibit 4?

(Whereupon, Exhibit No. 4, Handbook of Toxicological Pathology, Chapter 47, "Kidney," was marked for identification.)

MS. ALTHOFF: That's pretty. I don't think that was my 29.

Ah, there we go.

BY MS. ALTHOFF:

Q And I'll -- I'll let you download this if you'd like --

A Yeah.

Q -- Doctor.

But do you recognize this document that's been marked as Exhibit 4 as Haschek and Rousseaux's textbook on toxicologic pathology, and particularly the chapter on kidney?

MR. PENNOCK: The doctor is opening up the exhibit now.

BY MS. ALTHOFF:

Q Were you able to open it, Doctor?

A Yeah. Yes, I was.

Q And do you recognize this as Haschek and Rousseaux's Handbook of Toxicologic Pathology, particularly the "Kidney" chapter?

A Yes, I do.
Q If we look at the second page, and the first column, the second full paragraph --
MS. ALTHOFF: If we could blow that up. It starts with, "In the safety assessment."
Okay. That's good.
A Yeah.
BY MS. ALTHOFF:
Q And, Doctor, does this say, "In the safety assessment of new molecular entities, the concordance in response to xenobiotics in rat and human strongly supports the rat as a good predictor for human renal hazard. The exceptions in concordance include two categories: Immune-mediated drug injury in humans."
Do you see that?
A Yes.
Q And the second one was: "And the xenobiotic-associated unique alpha2µ-globulin nephropathy syndrome in male rats."
Do you see that?
A Yes.
Q Do you agree with this statement in Haschek and Rousseaux's?

A I do not agree, no.

Q All right. And why is it that you don't agree with Haschek and Rousseaux's treatise on toxicologic pathology with regard to its statement that although rats can be a good predictor of human renal hazard, an exception to that is immune-mediated drug injury in humans?

A Because I believe that drug-induced immune lesions such as inflammatory interstitial infiltrate can be induced in rats by -- by drugs.

So the rat, in my opinion, can be used as a model for a drug-induced inflammatory infiltrate of the kidney.

Q Do you have any disagreement with Haschek and Rousseaux's statement that the human rat concordance is not helpful where it's a xenobiotic-associated unique alpha2µ-globulin neuropathy [sic] syndrome in the male rat?

A Yeah. I have not worked with that syndrome in rats. So I cannot really comment on that.

Q And you weren't even aware that it's only in male rats; correct?

A I -- as I said, I -- I am not very familiar with the alpha-2 globulin nephropathy in

rats.

Q All right. Let's go back to your report, Exhibit 3, and page 7. All right. Yeah.

So that first paragraph, Dr. Moeckel, under "AstraZeneca Nonclinical Studies," does that describe the methodology that you used to review the preclinical and nonclinical data that you received from AstraZeneca?

A Yes.

Q And your report, which is on the screen, but also marked as Exhibit 3, includes all of your opinions that you have, as you sit here today, regarding the AstraZeneca preclinical studies; correct?

A Again, you have to repeat. There was noise in the background.

Q Sure.

So your report, which is Exhibit 3, and it's -- part of it is on the screen today, includes all of your opinions regarding the AstraZeneca preclinical studies that you formed as you sit here today?

A Yes.

Q And according to this section on page 7, you received 20 slides from 20 preclinical

studies from AstraZeneca; is that correct?

A Yes, I believe that is correct.

Q In fact, I -- the number is not there. It's typewritten out. If you see that in your first sentence, Dr. Moeckel, it says, "I received 3 external hard drives." And it talks about the number of images from a variety of experimental animals from 20 preclinical studies.

Do you see that?

A Yes, I see that.

Q And that's correct; yes?

A Yes. Yes.

Q Okay. When you received those slides from the 20 preclinical studies, at the time you received those slides, you had already received AstraZeneca's preclinical or nonclinical study reports; correct?

A That is correct.

Q And you had already done some level of review of those reports that you had received prior to getting the slides?

A That is correct.

Q And am I correct, Dr. Moeckel, that you, in fact, identified which of the preclinical studies from AstraZeneca that you had received

reports from that you wanted slides for if they were available?

A Yes, that is correct.

Q So at the time you received the slides, you were not able to do a blinded review of the slides; correct?

A Well, I would say that I -- when I looked at the images, the images were organized on the drives in control and non-control. And in some images, they had concentration of the PPI drug use.

So in that respect, I could not be completely blinded.

Q And you had already reviewed the study reports that related to those slides at the time you received the slides?

A Yes.

Q Would you agree, Dr. Moeckel, that it causes a certain level of bias when you know what the slide -- whether the slide is from a dosed group or a control group before you look at it?

MR. PENNOCK: Objection.

A No. Actually, I -- I don't agree at all that it concludes bias.

The number of slides were so many

that -- and -- and I -- I knew from the investigator's report that there were changes present and, more importantly, that there were even kidney sections available, because on -- not on all studies were kidney sections available. So that was one selection criteria, that I chose those studies that had kidney sections available.

But the only bias that I would have is that the investigator of the study mentioned that there was some change in the histology of the kidney, but I did not know to which nature the change was, and also the histological descriptions by the study investigators were so general and sometimes so superficial without enough detail that I often could not necessarily have any kind of assumption what I would be seeing in the respective kidney tissue slide.

BY MS. ALTHOFF:

Q As you were looking --

A So I --

Q I'm sorry.

A Uh-huh.

Q Go ahead. You finish.

A Well, I don't -- I don't feel particularly biased. I -- I just looked at all

the images as I got them.

Q And you said at the time you were looking at the slide, you did not know the -- the nature -- I'm -- I couldn't quite hear you.

A Yeah. Yeah.

At the time when I looked at the image files on the drive, I only could tell that they were from control animals or they were from animals that were in the drug group. But I would not know a priori which digital slide would actually show pathology.

Q Is it your understanding, Dr. Moeckel, that when a animal pathologist is reviewing histological pathology slides during a study of a drug, you know, prior to approval, that that toxicologist or animal pathologist does not know whether the tissue its looking at is from a dose group or not or what dose group?

A Well, if -- if the animal tissue pathologist was conducting the study, if -- if that person is truly blinded, then he or she would not know whether the kidney section is from a control or from a drugged animal.

But, you know, there -- the prerequisite for that is that it is truly a

blinded study, and I am not aware that that is always the case.

Q When you -- as you were reviewing the slides from AstraZeneca's nonclinical studies, as you reviewed the slides, were you also looking at the study reports contemporaneously?

A No, I did not.

I reviewed the slides just as they were on the drive, and I only evaluated them for what I thought were pathological lesions. And I did not have the report open at the side of my computer to refer to.

Q When you were identifying what you thought to be the pathological lesions on a particular slide, would you identify all the pathological lesions or were you only looking for specific ones and noting specific ones?

A No. I would always look at all pathologic lesions that I could possibly identify.

Q And I think this is assumed, but I just want to make sure. We're only talking about kidney slides; correct?

A Yes. I only examined kidney slides.

Q When you were determining which studies to request -- well, strike that.

You only requested a subset of what could be potentially available pathologic or histopathologic data -- let me strike -- let me start this over.

You decided, after reviewing study reports again, which studies to choose to see slides from; correct?

A That's correct.

Q And you didn't ask to see every potential study that might be available?

A As you know, there are so many studies with so many animal data and -- and tissue sections that it was not practical to look at all studies.

So, yes, I selected studies that I felt were important to look at that was based on a number of different criteria, including the way the drug was given, the lengths of the study, the animal species, whether the report mentioned changes in either a kidney function or histopathological lesions mentioned in the report.

So I had a number of criteria that I used to decide which of the many studies I wanted to look at.

Q And I think specifically on page 6, you

state, "I reviewed the reports described above and identified lesions in the kidney that occurred in greater numbers and in greater degrees of severity in the dosed animals versus the controls."

Correct?

MR. PENNOCK: Objection to form.

A Uh-huh.

BY MS. ALTHOFF:

Q It's the first sentence on -- of that paragraph that's on the screen, page 6.

A Uh-huh.

MR. PENNOCK: Objection.

BY MS. ALTHOFF:

Q Is -- I'm sorry. Are you waiting for another question or have you answered?

A No. I -- I'm -- I'm just rereading the paragraph for a second; yeah?

Q No. That's fine.

A Yeah. So that was a -- as is described in that sentence, that was a criteria, because I was curious to see whether the pathological lesions that were described by the study pathologist were consistent with what I would evaluate those lesions for.

So I basically wanted also to review

the pathological lesion to get an impression of how adequate was the pathological evaluation.

Q So for example, you did not request to see studies where there were no reported kidney findings?

A I -- I do not remember off the top of my head whether I did not request any of the -- there might have been studies that I requested that had no description of pathologic lesions, but where I was interested, because, for instance, the studied animal was a, you know, very junior one or the study was a particular way of application that I thought was important to review.

Q Well, were there any studies, Dr. Moeckel, that you discussed in your report, Appendix A or Appendix B, in which you found kidney findings that you felt were significant to report as it relates to your opinions in this case, but that AstraZeneca reported no kidney findings at all?

A Yes.

Q Which study was that?

A I would need to find that. I -- that would -- that might take some time.

Q Well, Dr. Moeckel, let me ask you this:

Would that be significant to you such that you would discuss it in your report if you reviewed the slides or images from a study you saw kidney findings and AstraZeneca said there were none?

MR. PENNOCK: Objection to the --

A Yeah. So as far as I remember, there were several studies where no pathologic lesion was described, as far as I remember, but where I saw pathology on the histological sections.

BY MS. ALTHOFF:

Q Where in the body of your report do you discuss studies where you identified kidney findings in the slides and AstraZeneca said there are no kidney findings?

A So I would need to review in the appendix probably --

Q Would that be Appendix --

A Yeah.

Q Well, let me -- let me ask you this, Dr. Moeckel: So Appendix A are studies where you asked to see the renal slides, and they were produced; correct?

MS. ALTHOFF: That's going to be, like, page 31 --

A Uh-huh.

MS. ALTHOFF: -- Jeff.

A Uh-huh.

BY MS. ALTHOFF:

Q Is that correct, Doctor?

A Yeah.

Q Okay. And so Appendix B is, in fact, studies where you didn't review any slides? You just reviewed the study report; correct?

MR. PENNOCK: Objection.

A I believe that's correct.

BY MS. ALTHOFF:

Q If you look at --

MS. ALTHOFF: So that would be a couple more pages down --

A Uh-huh.

MS. ALTHOFF: -- Jeff. We can just verify that.

BY MS. ALTHOFF:

Q So Appendix B, it says: AstraZeneca Studies: Renal Slides Requested but Not Received. Do you see that?

A Yeah.

THE WITNESS: Can you enlarge the image, please?

BY MS. ALTHOFF:

Q So my question to you, Doctor, is --

A Yeah.

Q -- if you saw something on a slide that you're contending AstraZeneca did not put in its report, it couldn't be in Appendix B, because you didn't review any slides or any of the studies on Appendix B?

A Yeah.

No. No. I -- that is correct.

Q Okay. So you were interested in whether Exhibit A might contain something where you saw something on the slide and AstraZeneca reported nothing.

MS. ALTHOFF: So let's mark as -- Appendix A, which is my 3, Jeff, as the next exhibit.

(Whereupon, Exhibit No. 5, Appendix A, was marked for identification.)

MS. ALTHOFF: So we're showing on the screen Appendix A, page one.

And if you could pull up both pages, that would be helpful, Jeff.

THE WITNESS: Uh-huh.

MS. ALTHOFF: No. I meant -- I'm

sorry. I meant the next page.

Yeah. That page and the page before it. So pages two and three of this exhibit.

THE VIDEOGRAPHER: If you want to give me just a second, I can get that done, but I don't have that --

MS. ALTHOFF: Yeah. Sure.

THE VIDEOGRAPHER: -- software that'll do it easy.

MS. ALTHOFF: Oh, sorry.

THE VIDEOGRAPHER: Just give me a sec.

BY MS. ALTHOFF:

Q Well, Dr. Moeckel, do you have Appendix A in front of you?

A Yes, I do.

Q Okay. Well, while Jeff is working on this on the screen, can you identify any of the studies that are listed on Appendix A, which is the current exhibit, for which you found kidney findings on the slides and it's your contention that AstraZeneca said there were none?

A So I would like to modify my answer in that respect, that the things that I -- the -- the

pathologic lesions that I identified on these studies were not in that degree mentioned in the AstraZeneca study reports.

So what I'm saying is they may have mentioned something, likely chronic progressive nephropathy, but they in my opinion did not evaluate and did not describe and assess the lesions that I saw adequately.

Q All right. I think we're on the same page. I just want to make sure, Dr. Moeckel, that you weren't contending that AstraZeneca said there were no kidney findings in some of these studies.

Understood. All right.

Going back to your methodology, Dr. Moeckel, that we've been -- we were talking about before we kind of went down this rabbit hole, you asked to see the slides or kidney tissue from certain studies to the extent available; correct?

A Yes. Yes.

Q And you were -- I'm sorry.

You were aware, at the time you made that request, that many of these studies were old?

A Yes.

Q And you were aware and understood that

often tissue is not retained from studies that are that old?

A So I was actually surprised that some -- in some studies that I requested slides for, no slides were produced. I'm not aware of any excuse that AstraZeneca used not to produce these slides, like, for instance, the studies were so old.

In my opinion as a physician and scientist, if you do such an important study like a drug toxicity study, in my opinion it would be prudent and good practice to keep the tissue blocks ad infinitum in order to review if any kind of question regarding the integrity of the study or the analysis of the study comes up.

As you may know, in hospitals we keep blocks of tissue at least ten years, and Yale in particular has blocks stored that go 30, 40 years back.

So I was negatively surprised that AstraZeneca could not come up with all the tissue slides that I had requested.

Q Dr. Moeckel, do you have an opinion with regard to what the regulatory requirements are for maintenance of tissue for a drug that was

approved in the '90s?

A Well, in my opinion, I think it would be the adequate practice to have blocks available of the tissue that was used in a animal toxicology study in the '90s. That's not that long ago.

Q Do you know what the regulatory requirements are for maintenance of tissue blocks from animals for studies done -- for toxicology purposes for drugs that are approved by the FDA?

A I would assume that they should be responsible to keep these blocks for a very long time.

Q That's not my question, Dr. Moeckel.

My question is: What is the regulatory requirement for maintenance of tissue and tissue blocks or slides even from studies that were submitted to regulatory bodies, including the FDA?

A Well, I would assume it should be at least 20 or 30 years.

Q But that's an assumption on your part? You don't know?

A That's what I would think as a minimum ethical conduct.

Q Again, I asked you, Dr. Moeckel, if you knew what the FDA requires with regard to

maintenance of tissue blocks, slides, other tissue samples from animal studies that were done to promote -- or to prepare for a drug approval?

MR. PENNOCK: Okay. Just note my objection. He's not offered any opinions regarding regulatory matters or regulations. And he's given you an answer several times as to what he thinks the company should have done regardless of what the cop on the street was telling the company to do.

BY MS. ALTHOFF:

Q You can answer, Dr. Moeckel.

A Yeah. As I said before, I assumed that the regulatory regulations would guarantee blocks to be stored for at least 30 years.

Q All right. Let's move on.

MS. ALTHOFF: Actually, let's take another break. It's about 1:30. So I think we've been going another hour or so.

And do we -- Dr. Moeckel, I don't know what your situation is with lunch, etc., but we're happy to accommodate your schedule.

MR. PENNOCK: Well, we have -- you know, we -- I know you have six hours of time. We're -- we have this room until 6:30, which should be more than adequate so long as we don't take too many breaks.

MS. ALTHOFF: Okay.

MR. PENNOCK: So if you want to take a break, of course, we'll agree to that.

Could I ask the videographer to please tell me how much time we have on the record right now?

Well, let's go off the record and -- as we're taking a break, and tell me how much time we have on the record.

THE VIDEOGRAPHER: Off the record 1:29 p.m.

(Whereupon, there was a recess taken from 1:29 p.m. to 1:47 p.m.)

THE VIDEOGRAPHER: On the record 1:47 p.m.

BY MS. ALTHOFF:

Q Dr. Moeckel, we're back on the record.

And when we went off the record, we were talking -- there we go -- about the methodology that you used in reviewing the internal data that you received from the PPI manufacturers.

Do you recall that, generally?

A Yes.

Q So in looking at the body of your report, Dr. Moeckel, where you go through and discuss individually the AstraZeneca studies that you reviewed, I note that there are photographs of certain slides of certain animals; correct?

A Yes.

Q Did you make images of any other animals other than what is depicted in your report?

A No.

Q As you were doing your review of the individual slides -- and I know you said you reviewed something like 1100 slides; is that right?

A Yes.

Q -- did you keep contemporaneous note or a log of the slides that you reviewed?

A No.

Q How did you memorialize the review that you did of the individual slides?

A So I -- I took the -- the image, and then I wrote in a -- a footnote what I saw. And what I then did was I took the image and put it into a PowerPoint presentation and also wrote a legend for each image with the pertinent findings.

Q So -- make sure I understand this.

So there's 1100 slides. And when you pull up slide No. 1 from the first study on the first drive, how do you memorialize, if at all, what you see on that slide?

A So I -- I memorize it, and I go through the respective slides in the respective studies. And when I screen the slide and I see a pathologic lesion, then I would take a -- a photo or a snapshot of that lesion, and that then became this image.

Q Gotcha.

So as you would go through a study -- I'll -- for example, T 1636, which was the two-year rat study from AstraZeneca, you would go through each of the slides that you received from that study, identify any of those which you thought had a pathological lesion and sort of

screen shot -- shot or somehow capture the image from that particular animal in that study?

A Correct.

Q And so then, do I understand correctly then that the only slides that you took images of as it relates to the AstraZeneca nonclinical studies are the ones that are contained in your report?

A Yes.

Q So for example, with regard to the studies that are summarized in Exhibit A where you had slides, but they didn't make it into the body of your report -- you're familiar with that -- Appendix A; right?

A Yeah, yeah, yeah. Uh-huh.

Q And you included a summary of observations --

A Right.

Q -- with regard to the studies in each category, but you did not include any photographs there; right?

A Right.

Q And how did you memorialize, if at all, which animals from the various studies on Appendix A had the lesions that you've summarized in your

summary of observations?

A Yeah. So for -- for those -- so let me see whether I am here in the right appendix. One moment.

Q Uh-huh.

A Appendix B. Okay.

So your question was these studies in Appendix A where I reviewed slides, but I did not include images, in -- as I said, in -- in those studies, I would create these comments and add them to this report.

Q Okay. So let's just look at a couple of examples.

So under your "3 month/13 week," "Rat" section --

A Uh-huh.

Q -- you have a summary of observations that includes calcium crystal precipitations and other signs of acute tubular injury in dosed omeprazole combination groups; correct?

A Correct. Yes.

Q And then underneath that, you cite one study, which is 96153, "Omeprazole/Amoxicillin/Metronidazole" -- can't say that -- "combination: 3 month oral toxicity in

the rat."

So you only cite one study there; correct?

A Yes.

Q Do you have memorialized anywhere which of the animals in 96153 you observed the calcium crystal precipitations and other signs of acute tubular injury?

A So I do not remember exactly which particular animal it was.

Q Okay. Looking at the second sort of topic there, it's again under the "Rat," "One month or less."

A Uh-huh.

Q And you list your summary of observations.

A Uh-huh.

Q Including tubular basophilia, calcification, vacuoles, acute tubular injury, casts, apical blebbing in dosed groups.

A Uh-huh.

Q And then you list three studies after that; correct?

A Uh-huh.

Q Did you see all of those observations

in each of those studies?

A Yes.

Q And did you memorialize anywhere the animals in which you saw those observations in those three studies?

A I do not remember the individual animal in each group where I saw that, and I usually -- what I did was that I saw these changes in several of the animals in the study group. You know, this is what I wrote. In dose groups, I saw these lesions.

Q Okay.

A Uh-huh.

Q And, again, I'm just trying to find out what -- what you did, Dr. Moeckel, and if there's additional documents out there or information.

So going back to your report, there are a number of studies that you discuss in the body of the report aside from the Appendix A, and in those studies you -- in -- I think in all cases, discuss particular animals by -- by number?

A Right.

Q And with regard to the, you know, summary of that study and what you saw, you know, generally with regard to your observations in that

study, were those findings exclusive to the animals that you identify specifically?

A No. They were not exclusive to the animal from which the picture is taken. The picture is taken from the respective animals, if you can look up in the report, but there were other animals in that group that also had similar lesions.

So basically, I used the image as a representative image of the lesion that I saw.

Q And did you memorialize anywhere the other animals where you saw the same or similar lesions?

A So I did not memorize all of the numbers of these other animals, but certainly if I or somebody else went back to that group and looked at that group, they would find these lesions.

Q And you're using the word "memorize," and I'm using the word "memorialize." I want to make sure we're speaking the same language.

I'm asking you: Did you write down any data about other particular animals?

A No, I did not.

Q Okay. In terms of the observations

that you made in these studies when you looked at specific slides, Dr. Moeckel -- so, for instance, you might have observed basophilia, for instance --

A Right.

Q -- did you grade the severity of those findings and memorialize that anywhere?

A No, I did not grade. I'm aware that there is a grading system that some authors have developed, but I only used in my descriptive assessment mild, moderate to severe, which is usually the grade that we use on kidney biopsy lesions.

Q Did you include in your report, when you would describe your findings, those terms, "mild," "moderate" or "severe"?

A So I believe that you can find descriptors, like, extensive, you know, that is in regard to the amount of tissue involved, but I -- I do have qualifiers for the different lesions that I have used. I have -- so for instance, you know, extensive injury, and I believe I have also used other qualifiers as focal versus diffused.

So those are just general histopathological descriptive terms that we use in

practice every day and with whom I'm very familiar with.

Q I just forgot my question, but -- oh. When you identified a lesion on a particular slide for a particular animal in a particular study, did you make an effort to cross-reference that same animal in the AstraZeneca preclinical study report to determine whether AstraZeneca's clinical investigators had identified the same lesion and how they graded it?

A So in some studies, I believe I did. I did not do it in all studies or all lesions that I did -- that I discovered.

Q Do you recall which studies you did that cross-comparison?

A Off the top of my head, I cannot immediately remember.

Q Uh-huh. Specifically, if you look --

MS. ALTHOFF: If we go to Exhibit 3, which is his report, page 8 -- well, let's start at page 7.

A So page 7 in my report, is that the -- is that what --

BY MS. ALTHOFF:

Q Yes, Doctor.

A Uh-huh.

Q The bottom -- towards the bottom of that page is where you begin talking about Study T 1636, which is the two-year chronic rat study; correct?

A Yes.

Q And then if you turn the page, which -- so page 8, you have a number of bulleted items; correct?

A Yes.

Q And, in fact, these bulleted items, although not verbatim, were included in the study report; correct?

A Yes. They are written in -- on page 8 in the study report.

Q Maybe you didn't understand my question.

A Yeah.

Q So --

A Sorry.

Q No. That's okay.

So these bulleted items that you have included in your expert report, which is

Exhibit 3, were also included, albeit not verbatim, in AstraZeneca's nonclinical study report; correct?

A Yeah. They were -- yeah. Yes, that's right.

Q Did you have additional lesions that you identified in T 1636 that were not included in that bulleted list?

A Give me one second.

So what I saw, which was particularly concerning, was the fact that in the drugged animals, there was significant acute tubular injury.

Q Okay. And was the acute tubular injury otherwise described in those bulleted -- the bulleted list?

A No.

Q So when you describe tubular injury, you say in your report that it's "manifested by extensive proteinaceous casts, flattened tubular epithelium with nuclear drop-out and with sloughing of brush border in individual hole without the 'apparent thickening of glomerular and tubular basement membranes.'"

Am I understanding that correctly?

A Yes.

Q Okay. So, again, by "tubular injury," you're talking about it being manifested by those items I just read?

A Yes. Especially, the sloughing of the epithelial cells and the dilated lumen and the nuclear drop-out. So all the pertinent features that are well known as acute tubular injury.

Q And are those same items of acute tubular injury have been described as elements of chronic progressive nephropathy in rats?

A No, they have not.

Q And you identify a couple places in your report that you expected to see conspicuous thickening of the glomerular basement membrane; correct?

A Can you show me where I said that?

Q Sure.

So specifically on page 9 in that section we just read, so in the quotes. Do you see that, Doctor, where it says "apparent thickening of the glomerular and tubular basement membranes"?

A Yeah.

Q Okay.

A I see that.
Q Well, first of all, why is that put in quotes?
A Because I want to emphasize that the apparent thickening -- or the thickening of the glomerular and tubular basement membrane was not seen in these lesions.
Q Okay. I was trying to figure out what you were quoting.
Were you quoting directly from something there?
A No. I --
Q Okay.
A I was just referring to that there is no -- and I wanted to point out that there's no thickening of glomerular and tubular basement membrane thickening.
Q Is it your opinion, Dr. Moeckel, that thickening of the glomerular basement membrane is required for a diagnosis of CPN?
A Yes.
Q And what is your basis for your opinion that the apparent thickening of the glomerular basement membrane is required?
A So chronic progressive nephropathy is a

spontaneous chronic lesion that develops in old rats. And the pertinent finding is that of thickened basement membrane, glomerular basement membrane and tubular basement membrane, and also glomerulosclerosis. That is actually, in the original descriptions, the key finding that characterizes chronic progressive nephropathy in elderly rats.

However, the lesions that I saw in this study were not at all chronic -- they were acute -- and not at all showed any glomerulosclerosis and any tubular basement membrane thickness. Therefore, they do not show criteria of chronic progressive nephropathy, but rather of acute tubular injury.

Q And, Dr. Moeckel, at what stage in chronic progressive nephropathy does apparent thickening of the glomerular basement membrane occur?

A Well, that depends who you read. You know, there are some authors who say it is part of the chronic progressive nephropathy when it develops in elderly rats. There are some authors who say you should not call a lesion chronic progressive nephropathy if you do not see tubular

basement membrane or glomerular basement membrane thickening.

And there are some authors who say it can even be seen in the early parts of CPN, although authors differ in their opinion when early CPN begins. Some say at about 18 months and beyond or 18 months would be the earliest CPN. But there are other authors who claim it can be seen earlier.

So in any ways, I think if you call a lesion chronic progressive nephropathy, you have to show thickened tubular basement membrane and thickened glomerular basement membrane and glomerulosclerosis.

None of these were visible in any of these lesions that I depict in my report.

Q Dr. Moeckel, which comes first, thickening of the tubular basement membrane or thickening of the glomerular basement membrane, in the normal progression of chronic progressive nephropathy?

A I think they can be simultaneous.

Q What's your opinion with regard to whether, in rats as young as 12 weeks, you can see lesions of early CPN?

A I disagree with that statement.

Q Do you agree that in -- chronic progressive nephropathy can be exacerbated by many chemicals?

A I have not, you know, seen studies or reviewed studies where that was definitively proven. I know that there are authors in the literature that claim that.

But I have not conducted studies to that respect or the papers that I reviewed, in my opinion, did not show convincingly that drugs can exacerbate chronic progressive nephropathy.

Q Have you reviewed any studies from the National Toxicological Program?

A I -- I have reviewed articles, so summaries, but I have not reviewed the study material itself.

Q Have you reviewed any NTP studies where the chemical compound exacerbated chronic progressive nephropathy in the rats and was not found to be a risk to human health?

A I remember reading this, and I disagree with that statement.

Q So you disagree with the findings from the National Toxicologic Program?

A I disagree with the quote of exactly that statement that I read in an article.

Q Do you know what article that was where you read that?

A I don't know off the top of my head, but I can find that article for you.

Q One of the articles that you cite in your report is the Frazier 2012 article, Frazier and Seely's "Proliferative and Nonproliferative Lesions of the Rat and Mouse Urinary System."

I believe that was reference 1 to your report; correct?

A Yes.

Q And is that a piece of literature that you relied upon in reaching the opinions in your report?

A That was one of the papers that I read and reviewed to inform myself about the entity of CPN in the -- and general aspects of experimental toxicology animal models, yes.

Q And that particular paper was the result of a International Harmonization of Nomenclature and Diagnostic Criteria for Lesions in Rats and Mice; correct?

A Yes.

Q And that paper purports to set forth a standardized nomenclature for classifying lesions observed in the urinary tract to include the kidney of rats and mice; right?

A Yes, that's right.

Q Did you disagree with the standard nomenclature and the information set forth in that publication?

MR. PENNOCK: Objection.

Do you want to show him the paper?

A Yeah. Can -- can you show me the paper?

BY MS. ALTHOFF:

Q Sure.

A So we can maybe all take a look at this.

Q Sure.

MS. ALTHOFF: It's -- this would be my 9. We'll make that the next exhibit.

(Whereupon, Exhibit No. 6, "Proliferative and Nonproliferative Lesions of the Rat and Mouse Urinary Systems," was marked for identification.)

BY MS. ALTHOFF:

Q And the question, Dr. Moeckel, is: Do you recognize --

MS. ALTHOFF: What exhibit are we on, Reporter? Six?

THE VIDEOGRAPHER: This is 6.

MS. ALTHOFF: Six.

BY MS. ALTHOFF:

Q So you recognize Exhibit 6 as being reference No. 1 to your expert report in this matter, that being a article by Frazier and Seely entitled "Proliferative and Nonproliferative Lesions of the Rat and Mouse Urinary System," published in Toxicologic Pathology in 2012?

A Yes.

Q Okay. And my question was: Since you list this as a reference in your report, do you agree with the -- we'll start with the nomenclature that is set forth in this article which was the result of the International Harmonization of Nomenclature and Diagnostic Criteria for Lesions in Rats and Mice?

A So let me quickly reread the article to give you specific answers.

Q Well, I'd be happy to have you do that,

Doctor, but I think it's about 60, 70 pages.

A Well, I'm a quick reader.

Q Okay. Sure. Why don't --

MR. PENNOCK: Just ask him --

BY MS. ALTHOFF:

Q Did you download it, Doctor?

MR. PENNOCK: Just ask him if he disagrees with any of the nomenclature in the article.

I mean, without letting him read it, I don't know --

MS. ALTHOFF: It's --

MR. PENNOCK: -- how you expect him to answer.

MS. ALTHOFF: I -- I don't disagree with you, Paul, if this wasn't an article that was No. 1 on his reference list.

MR. PENNOCK: It's No. 2, but --

MS. ALTHOFF: Actually -- oh, you're right. I'm sorry.

It is No. 2.

MR. PENNOCK: Right.

MS. ALTHOFF: No. 1 was Seely and Frazier. Thank you.

MR. PENNOCK: It's not a memory test here.

BY MS. ALTHOFF:

Q Well, let me ask you a different question, Dr. Moeckel. We'll strike that question.

Do you recall, as you sit here today, having had any dispute with the nomenclature identified in Exhibit 6?

A So I remember that I was not agreeing with several items, but I would like to identify those for you.

Q Okay. Were those in the term of nomenclature or was that in terms of, like, diagnostic criteria?

A I will have to review these specific --

Q Okay.

A -- so that --

Q Let's take a little time and do that.

A Okay.

Q Doctor, have you had sufficient time to familiarize yourself with this document?

A Yes. Give me, please, one more minute.

Q Sure. Thank you.

A All right. So if you want to, we can

continue.

Q Sure. Thank you, Doctor.

So I think the question that I had asked you earlier, Dr. Moeckel, was whether there was a nomenclature that is discussed in Exhibit 6 --

A Uh-huh.

Q -- which is from the INHAND project, the International Harmonization of Nomenclature and Diagnostic Criteria --

A Uh-huh.

Q -- for Lesions in Rats and Mice --

A Uh-huh.

Q -- that you disagreed with?

A Yeah. So I disagree with the statement on page -- what is it? -- 27S.

Q Okay. Let's go to that.

A So --

Q It's about -- hold on just a second. It's about 12 pages in.

A Yeah. So there's this discussion about the early stages of CPN, and I personally do not agree that the early stages of CPN necessarily involve all of these features, basophilic tubals --

And I think that it is very easy to confuse tubular injury with early stages of CPN. So I -- I think that that is a little bit of a hyperbole in that nomenclature.

Q So if I understand what you're saying, Doctor, you disagree with using the term "chronic progressive nephropathy" or "CPN" in certain instances of early lesions in, you know, younger animals that reflect basophilic tubules with thickened tubular basement membranes, etc., as described in this report?

A Yes.

Q Do you have an opinion, Doctor, with regard to how old a rat has to be before you can diagnose it with chronic progressive nephropathy?

A So from my reading of the literature in the earlier papers, it was described as a lesion that is seen in rats usually 18 months or more in age.

Q And --

A So --

Q Sorry.

A Go ahead. Go ahead.

Q I'm sorry. I didn't mean to cut you off.

Are you finished?

A Yeah. I'm just repeating my answer.

Q Okay.

A So the age of CPN -- or the earliest age of CPN should be 18 months of age in a rat.

Q And --

A So -- okay. Go ahead.

Q And for purposes of what you're relying on there, you're looking at the three publications that you cite that were published in the 1970s, Couser, Gray, and Elema?

A You know, I cannot tell you it's specifically reference A, B, or C. I -- I have read dozens and dozens of papers about CPN, and I have noticed that in those papers that were written by authors that I think were nonbiased and independent, that they -- the initial description of the lesion was that in animals of 18 years -- 18 months or older.

Q And --

A And remember, the life age -- lifespan of a rat is about 24 to 26 months. So, you know, 18 months is certainly, in our definition of a lab animal that we use for experiments, an old animal.

Q And which authors did you not credit as

heavily because you thought they had some sort of a bias?

MR. PENNOCK: Objection.

A Yeah. Again, I'm sorry. I cannot tell you that off the top of my head, but I can certainly provide you that information if you want it.

BY MS. ALTHOFF:

Q Looking at what's on the screen -- so this is, again, going back to Exhibit 6, Frazier 2012, and that top right paragraph about halfway down, do you see it says, "CPN can be exacerbated by many chemicals that result in increased incidence and severity in chronic toxicity studies"?

A Let me quickly read.

Q Yeah.

MS. ALTHOFF: Jeff, can you highlight that? You're right there.

A Yeah. So I -- I see that they wrote this.

The problem that I have with this sentence is that if this -- if -- if you use a loose definition like that and say, oh, CPN can be exacerbated by many drugs, and the signals like

tubular basophilia is something that you also see in early drug injury, how can you ever differentiate a drug-induced real injury signal from, oh, it's just CPN?

And that is my problem with this part of the definition, that I think it is not -- it is too general, and it basically creates in the term "CPN" a wastebasket into which any kind of drug toxic injury can be put.

Basophilia is a well-known change in the tubular epithelial cell due to drug toxicity, due to any kind of heavy metal toxicity in use as it -- so it's -- it's a -- it's a injury sign.

But if you say, oh, you know, you can see that in early CPN, then you are off the hook. You are much better -- you cannot distinguish anymore what is a true injury signal versus just CPN.

And this is what I disagree with, with this whole assessment of CPN can start in two months' old rat as a chronic progressive aging lesion, and it has basophilia. And basically from then on, anything you see as an injury signal in the tubal can be basically put under the umbrella of CPN and doesn't concern us.

I think this is scientifically flawed. This is completely wrong.

BY MS. ALTHOFF:

Q Are you finished with your answer?

Let's go back a page to -- since you raised tubular basophilia. So this would be page 25 and 26S.

A Okay.

MS. ALTHOFF: So let's go back one more quickly, Jeff, so we can see where it starts.

Yeah. 25S.

BY MS. ALTHOFF:

Q So if you look at the bottom right, is that the section of this medical literature regarding basophilia, tubular?

Do you see where the word "Basophilia, Tubule" is on this page?

A Yeah. I see that.

Q Okay.

A Can you repeat your question, please?

Q That -- that was really my question. So I just simplified it.

Let's go to the next --

A Okay.

Q -- page so we can look at the rest of this section.

A Uh-huh.

Q And under the "Comment" section on basophilia, tubale, do you see where the consensus group has identified that -- several lines down -- "In young growing rats, a few basophilic cortical tubules are a normal feature"?

Do you see that, Doctor?

A I see that sentence, yes.

Q Okay. And do you disagree with that sentence?

A Yes, I do.

Q Okay. And if we go down a little bit further, there's the word -- it starts with "it."

It says, "It is commonly associated with CPN" -- so "it" being basophilia, tubale -- "coinciding with thickening of the basement membrane and occurs as a background change in an increasing percentage of rats and mice with age."

Do you see that?

A Yes.

Q Do you disagree with that sentence?

A So I agree that tubular basophilia can represent tubular regeneration, but may also

indicate early atrophy or persistent low-grade toxic injury.

Q With regard to chronic progressive nephropathy, do you disagree that that disease in rats is spontaneous in origin and of unknown etiology?

A Yes.

Q Do you agree the earliest detectable lesion of CPN in young adult rats is a basophilic tubule or evidence of regeneration in the outer kidney?

A Sorry. Can you repeat the question? There was again some acoustic breakup.

Q Sure.

Do you agree the earliest detectable lesion of CPN in young adult rats is a basophilic tubule or evidence of regeneration in the outer kidney?

A No, I don't, because I don't think that a young adult rat should have CPN.

Q With regard to granular or hyaline casts, do you agree those are features associated with chronic progressive nephropathy?

A Can you show me where that is written, please?

Q Sure.

So if we go forward a couple pages to 27S, you will see the section on "Casts." Do you see the word "casts" there on the screen --

A Yes.

Q -- Doctor, on your right?

A Yes, I do.

Q Uh-huh.

And going down, you see it refers to both granular and hyaline?

A Yes.

Q If you go down, it says "hyaline and granular" on the next page.

Do you see that?

A Yes.

Q Uh-huh.

And under the "Comment" section --

MS. ALTHOFF: Going down further, and about -- oops, don't go too far.

BY MS. ALTHOFF:

Q -- a few lines down, do you see where it says, "Casts are a common feature accompanying chronic nephropathies in rats and mice and their numbers increase with advancing age"?

A I agree with that sentence.

Q All right. Again, going back to the methodology you used to review the slides and prepare your report -- and, again, I'm referring to the internal AstraZeneca preclinical studies here -- we've talked about the fact that you didn't uniformly use a grading scale to evaluate the slides; correct?

A Correct.

Q Did you identify anywhere in the report the -- the sort of incidence of the lesions that you identify -- in other words, one seen in a female dosed group, zero in the controls, two in the controls, three in the dose groups, anything like that?

A No.

Q All right. Going back to Exhibit 3, which is your report, again in the body of your report, you discuss 8 of the 20 studies from which you had received slides from AstraZeneca; correct?

A Correct.

Q So you have four -- three chronic studies. So that being a study of more than a year on omeprazole; correct?

A Correct.

Q And you have no chronic studies on

esomeprazole in your report; correct?

A Correct.

Q And you have three studies that are subchronic. So 13 weeks to one year; correct?

A Yes.

Q And two of those were on omeprazole and one was esomeprazole?

A Yes.

Q All right. And finally, less than three months. So acute studies. You have two studies, one in a rat on omeprazole and one on a dog in esomeprazole; correct?

A Yes.

Q All right. So then let's look back at Exhibit A, which is -- I'm sorry -- Appendix A, which is Exhibit --

MS. ALTHOFF: Yes, that one.

Thank you.

BY MS. ALTHOFF:

Q And, again, we talked about the fact that this briefly addresses an additional 11 studies from which you received slides; right?

A Right.

Q All right. So under the three-month rat study, the only study you have listed there is

a three-month rat study, but it's in combination with an antibiotic and antifungal; correct?

A Yes. Correct.

Q And antibiotics are known to have kidney impact; correct?

A Antibiotics can cause kidney injury, yes.

Q Do you know why Study 96153 studied omeprazole in combination with amoxicillin and metronidazole?

A Can you repeat the question, please?

Q Sure.

Do you know why this study wasn't on omeprazole alone, but instead was on a combination with amoxicillin and a fungicide?

A I assume they wanted to test any kind of combined-drug injury or augmentation of drug injury when these other drugs are given.

Q Do you know why those other drugs are given in combination with omeprazole?

A I assume to treat patients with infections and at the same time have a proton-pump inhibitor.

Q So then looking under the one month -- or excuse me -- I'm losing my voice here -- the

three-month dog study --

A Uh-huh.

Q -- which is -- I'm trying to find it here. Oh.

Under the dog studies, three months, study 12PD [sic] is a three-month dog esomeprazole study using degraded esomeprazole pellets; correct?

A Yes.

Q Is there anything about the presence of the degradation products in that study that you're relying on?

A Can you please repeat the question?

Q Uh-huh.

Is there anything about the presence of the degradation products that were being studied in 1211PD that you're relying upon to reach your opinions in this case?

A So I'm not sure I understand your question. Can you repeat it one more time, please?

Q Yeah. Sure. Let me try to rephrase it.

A Yeah.

Q So we looked at the three-month dog

study, 1211PD, entitled "Esomeprazole Magnesium: 3-Month Toxicologic Qualification Study of Degraded Esomeprazole Pellets Given Orally to Dogs."

Correct?

A Yes.

Q All right. So in this particular study, they were not studying esomeprazole in its normal state? They were studying it degraded; correct?

A Correct.

Q All right. Is there anything about the presence or use of the degradation products in that study that you're relying upon to reach your opinions in this case?

MR. PENNOCK: Note my objection.

Go ahead.

A You know, I -- I -- I'm not sure I understand your question, to be honest with you. Can you rephrase that question maybe --

BY MS. ALTHOFF:

Q Uh-huh.

A -- or ask it differently?

Q Uh-huh.

Was there --

A I'm not --
Q -- anything about degraded esomeprazole versus nondegraded esomeprazole that had any effect on your opinions in this case?
A No. It did not have any opinion [sic] on my case.
Q All right. Let's look at Exhibit B to your report, which is your materials considered list.
MS. ALTHOFF: And that we will mark as the next exhibit. And it is my 6.
(Whereupon, Exhibit No. 7, Materials Considered by Expert Dr. Gilbert W. Moeckel, was marked for identification.)
MS. ALTHOFF: Hopefully, we can -- yes. Excellent.
BY MS. ALTHOFF:
Q All right. So, Doctor, have you reviewed this materials considered list --
A Yes. I --
Q -- prior to today?
A Yes. I did review that list.
Q Okay. And does it reflect all the

materials that you considered in reaching your opinions in this matter, in addition to the ones that are specifically cited by reference at the end of your report?

A Yes, they are.

Q All right. The first item listed there says the deposition, Carol Björkheden, October 10, 2019.

Did you review that deposition?

A I briefly read it, but I have not read it in its entirety.

Q Okay. So then fair to say there's nothing in that transcript that you're relying on for the opinions that are contained in your report?

A Yeah. I would say that is true.

Q With regard to the -- the labels for Nexium, Prilosec, and Protonix that are listed there, was there anything in those labels that you're relying upon in reaching your opinions in this case?

A Can you repeat the question again?

Q Yeah. Sure.

I -- I'm -- what I'm trying to find out, Dr. Moeckel, is if there are -- because these

items weren't specifically cited or referenced in your report, I'm trying to find out if there's anything in particular that are in these materials that you're, you know, relying on to reach your opinions, understanding that, of course, you know, you have the opportunity to review these materials; okay?

A Yeah.

Q And so my question was: With regard to the labels for Nexium, Prilosec, and Protonix, was there anything in particular in those labels that you're relying on to reach your opinions in this case?

A No.

Q There are a number of items that are listed with an AZ-KID-00-something --

A Right.

Q -- Bates number --

A Right.

Q -- which were internal confidential documents that were produced by AstraZeneca, but these, as I understand it, are not the studies which are down further in the list.

So was there anything in these nonstudy confidential documents that were produced by

AstraZeneca that you are particularly relying on in this case?

A No.

Q All right. Let's scroll down to the next section, which I think is the studies.

All right. So this section says, "AstraZeneca Conducted Non-Clinical Studies of Nexium and Prilosec."

And you, in fact, received study reports relating to the nonclinical studies of Nexium and Prilosec; right?

A Yes.

Q So were there studies that you received that didn't make it anywhere into your report, either in the body of the report or Appendix A or Appendix B?

A Can you repeat the question one more time, please?

Q Sure.

So this particular section of the materials considered list lists a number of studies, some of which say, "Renal Histopathology Slides" and some don't; correct?

A Right.

Q Were there any studies, such as listed

on this list, that you received for review that you did not include at all in your report, whether that be the body of the report, Exhibit A -- or Appendix A or Appendix B?

A So I -- I believe there could be some reports that I did not include, yes.

Q And how did you determine not to include a study report?

MR. PENNOCK: Just note my objection.

Not include it where?

BY MS. ALTHOFF:

Q Well, to the extent you did not include a study report anywhere -- yeah -- a discussion of it anywhere in your study -- your -- excuse me -- your expert report, whether it be the body, Appendix A or Appendix B, what criteria did you use to determine not to discuss that study in your report?

A So if the report did not show any description of a kidney renal failure, a pathological lesion in the kidney tissue, if -- for instance, in some studies kidney tissue wasn't even harvested and -- otherwise, the study model was not such that I would believe I needed to

review it because I was suspicious of possible toxic injury.

So in -- in other words, if there was no kidney tissue harvested and there was no evidence by serology that there was impaired kidney function, I -- that -- that could, for instance, be a criterion that I did not look at that study.

Q Okay. Let's look at page 6 of this report. So two pages down.

Okay. Let's see here.

About halfway down, do you see where it says "Study 276"?

A Yes, I do. Uh-huh.

Q And according to my records, Study 276 is entitled "Effective Long-Term Infusion of Omeprazole and/or PEG 400 on Renal Function in Rats."

Assuming that that title is correct --

A That --

Q -- do you have an understand- -- excuse me? Yeah?

A In what -- in what kind of animals? Could you --

Q Rats.

A -- repeat that, please?

In rats. Okay. Uh-huh.

Q Why would you have excluded a study from review that was entitled "Effective Long-Term Infusion of Omeprazole and/or PEG 400 on Renal Function in Rats"?

A I assumed -- and, you know, I've looked at dozens and dozens and dozens of studies and descriptions, but I assume that the parameters listed in this report did not show evidence of significant impaired kidney function.

So in other words, there was no scientific or pathologic evidence in the description of the report, in the summary of the report, that made me think I should look at those studies.

Q If you look one down from where we were just looking, Study 282 -- do you see that?

A Yes, I do.

Q Study 282 was entitled "Effective Long-Term Infusion of Omeprazole and/or PEG 400 on Renal Function in Dogs."

Is there a reason why you would not have discussed that study in your report?

A Again, I assumed -- without

remembering, because I looked at dozens and dozens of studies -- that when I reviewed the summary report and the report descriptions and results, I could not see evidence of impaired renal function. Therefore, I chose not to include that.

Q Did you have a time period of exposure that affected your selection of studies? In other words, were you interested in studies less than 13 weeks?

A Yeah. I was interested in studies that were short-term, and I also was interested in long-term studies. I was interested in studies in young animals. I was interested in studies in dogs and in mice.

So I had a very broad spectrum of criteria that I used to evaluate the impact of PPIs in animal models on the kidney.

MS. ALTHOFF: Let's go down one more page, page 7.

BY MS. ALTHOFF:

Q So if you look again about halfway down, do you see where it says, "Study 900544"?

A Yes, I do.

Q If that study is entitled "Esomeprazole Magnesium in 8-Week Oral Gavage Toxicity Study and

Toxicokinetic Study in the Neonatal and Young Adult Beagle Dog," is there a reason why you did not include that report in your study -- that report in your -- that study in your report?

A Again, I am certain that I reviewed the report summary, and I did not see evidence of kidney injury. And therefore, I -- since there was a limited amount of time to review all these studies that I wanted to review, I "choosed" -- I chose not to review this one because, again, in the model of the experiment, I did not see a strong signal regarding kidney injury.

Q And would your answer be the same for studies -- three-month oral studies on Beagle dogs and a three-month toxicity study in dogs --

A Which --

Q -- for why you didn't include those in your report?

A Which studies are those? I'm --

Q Sure.

So on page 7, Study 900715, and on page 7, Study T-1123.

MR. PENNOCK: Objection.

A Yes.

BY MS. ALTHOFF:

Q All right. Let's go down a little further.

MS. ALTHOFF: You can scroll down to -- oh, gosh, I don't -- I'm sorry. Keep going. It's -- keep going. Okay. Keep going a little further. Okay. Stop there.

BY MS. ALTHOFF:

Q Do you see at the top of page 13 out of 38 of this materials considered list, the two items that say FDA-1 and FDA-24?

A No. I think -- could you highlight that for me?

Q Sure.

If you look on the screen, it's there at the top before you get to "Literature."

A Yes. I see those. Yeah. Uh-huh.

Q Okay.

MS. ALTHOFF: Jeff, can you pull up what is my 28? And make this the next exhibit.

(Whereupon, Exhibit No. 8, Consult/Safety Review, Paolo Fanti, M.D., was marked for

identification.)

BY MS. ALTHOFF:

Q So, Dr. Moeckel, you're being shown what's been marked as the next exhibit. I think it's Exhibit 7 now. And this is an April 17, 2018 memorandum by Paolo Fanti from the FDA.

Do you see that?

A Yeah.

Could you please enlarge the --

Q Sure.

And my question, Dr. Moeckel, is just going to be: Did you review this memorandum? Because I can't tell what -- what FDA documents you reviewed.

MR. PENNOCK: Just note my objection. I mean, you're -- you're pulling out a document on his materials considered list.

So you switched from, is it included in your report or not included, to now review.

MS. ALTHOFF: I'm asking if he's reviewed it.

MR. PENNOCK: Well, it's -- Katherine, it's on his materials

considered list.

A Can you scroll down?

BY MS. ALTHOFF:

Q Uh-huh.

COURT REPORTER: Exhibit 8.

MS. ALTHOFF: Thank you.

A Yes, I did review this document.

BY MS. ALTHOFF:

Q Was there anything in this document that you relied upon in reaching your opinions in this case?

A I think that's almost impossible to say, since I reviewed so many documents.

That's -- that's all I can say.

Q Let's go to page 9, I believe, of this document.

MR. PENNOCK: Dr. Moeckel, do you -- do you want to take a break?

THE WITNESS: Yeah. I think I would like to take a break. I get paged the whole time here, and I could really --

MR. PENNOCK: You -- you probably haven't heard, but he's been getting pages. So he's going to have to --

MS. ALTHOFF: Okay.
MR. PENNOCK: -- just --
MS. ALTHOFF: All right. Well --
MR. PENNOCK: Let's take -- let's keep it as short as possible, 'cause our -- our last one ran almost 20 minutes, and we were back in our chairs in 11 minutes.
MS. ALTHOFF: Okay.
Let me ask you -- are you still here? Hello?
MR. PENNOCK: You got to put it back on.
Sorry. I didn't realize you shut it off.
Yeah. We're still here.
MS. ALTHOFF: Okay. All right. We can go ahead and take a break. Let's take ten. I'll probably be back sooner than that.
MR. PENNOCK: Or less; huh?
THE WITNESS: Yeah. A -- a five-minute break would be fine.
MS. ALTHOFF: Okay.
THE VIDEOGRAPHER: Off the record

3:02 p.m.

(Whereupon, there was a recess taken from 3:02 p.m. to 3:13 p.m.)

THE VIDEOGRAPHER: On the record 3:13 p.m.

MS. ALTHOFF: Jeff, I think we were on Exhibit 8?

Is -- is that the right number, Cliff?

THE VIDEOGRAPHER: Yes. This is 8.

MS. ALTHOFF: Okay.

BY MS. ALTHOFF:

Q Before we went on a quick break, Dr. Moeckel, I was showing you Exhibit 8, which you said you had received and reviewed, and then I was directing your attention to page 9 of that -- I don't know what you call it -- memorandum from the FDA. And that's what's up on your screen, which is a -- shows a picture of -- it says "Possible Mechanisms of PPI [sic] Nephrotoxicity."

Do you see that?

A Yes.

Q Have you yourself analyzed whether chronic kidney disease may be caused by the

biologic mechanisms set forth on page 9 of this report?

A I would need to see page 9, please.

Q That's what's depicted on the screen, Dr. Moeckel.

A Okay.

MR. PENNOCK: Again, I'm just going to note my objection to continuing examination regarding opinions not offered in Dr. Moeckel's report.

MS. ALTHOFF: Fair enough, Paul. That's kind of what I'm trying to --

MR. PENNOCK: Well --

MS. ALTHOFF: -- to rule out.

MR. PENNOCK: Who is this?

No. No. This -- this -- this schematic, why -- you're showing him things that have nothing to do with it.

Go ahead.

A Could you please repeat your question?

BY MS. ALTHOFF:

Q Have you, yourself, analyzed whether chronic kidney disease may be caused by the biologic mechanisms set forth on page 9 of this

report?

MR. PENNOCK: Same objection. No such opinions are being offered in this report.

Go ahead. You can answer.

THE WITNESS: Yeah. I'm just looking at this one more time.

A I believe these are possible mechanisms how PPIs can cause chronic kidney disease.

BY MS. ALTHOFF:

Q And my question, Doctor, was: Have you analyzed these potential mechanisms yourself?

A What do you mean by "analyze"?

Q Have you reviewed the underlying literature, if any, supporting or refuting these possible mechanisms?

MR. PENNOCK: Objection. No such opinions are being offered in this report.

Go ahead.

BY MS. ALTHOFF:

Q Well, let -- let's -- let me ask a different question.

Dr. Moeckel, would you agree that you're not offering any opinions in this matter

with regard to the possible mechanisms of PPI nephrotoxicity?

MR. PENNOCK: In humans?

MS. ALTHOFF: In humans, yes.

A No. Obviously, my review does not pertain to mechanisms of PPI-induced CKD in humans.

BY MS. ALTHOFF:

Q Okay. So let's go to Exhibit 3, which is your report, the "Analysis" section, page 25 and 26.

Starting at the bottom of page 25, Doctor, it starts, "Humans and animals share similar mechanisms of action leading to CKD from toxic tubular insults."

Do you see that?

A Yes.

Q And then it goes on to the next page, and it discusses an article by first author Yepuri. It says, "Yepuri, using human endothelial cells, demonstrated that chronic exposure to esomeprazole (but not to another H+/K+ ATPase inhibitor) led to an endothelial senescence linked to telomere attrition and oxidative stress."

Do you see that?

A Yes, I do.

Q And so despite these sort of statements in your report, Doctor, do you agree that you are not entering an opinion in this case with regard to the mechanisms by which PPIs may cause chronic kidney disease in human patients?

A No. In my report, I cannot show any kind of proof that a mechanism such as endothelial senescence may lead to CKD in humans. My report pertains to the injury in animal -- preclinical animal studies.

Q Okay. So you don't intend to offer any opinions at trial, Doctor, that what you saw on the animal slides in the AstraZeneca preclinical studies is the same mechanism by which PPIs can cause CKD in humans?

A I cannot voice an opinion about the exact mechanisms of PPI toxicity and role in CKD formation in humans because I have not studied human tissue in that respect.

I can only report about lesions that I see in rat and dog and mice kidneys that have the potential to develop to chronic kidney disease in these animals, and similar mechanisms are known to happen in humans.

Q When you say, Doctor, "I can only report about lesions that I've seen [sic] in rat and dog and mice kidneys that have the potential to develop chronic kidney disease in those [sic] animals, and similar mechanisms are known to happen in humans."

What similar mechanisms are you referring to?

A I'm referring to the known fact that acute tubular injury can lead to chronic kidney disease in humans, and that has been shown in clinical studies.

Q And with regard to acute tubular injury, you're referring to the studies with regard to AKI as a continuum to CKD?

A That's correct.

Q And are you aware of whether -- well, can you cite any studies, Dr. Moeckel, for the proposition that acute tubular injury in the form of acute interstitial nephritis has been studied specifically to determine whether it can lead to chronic kidney disease?

MR. PENNOCK: Objection.

A I don't know these studies off the top of my head, because I think it's beyond the scope

of this deposition.

However, I can provide you with references, if you want me to, after the deposition, and I'm willing to do that.

Q And I think in your report, Dr. Moeckel, you cited the Basile 2016 progression after AKI; the -- the Venkatachalam paper, 2010; and the Zuk and Bonventre paper from 2016, all with regard to AKI as a continuum to CKD; is that correct?

A That is correct, yes.

Q And none of those papers involved PPIs; correct?

A That is correct.

Q And as discussed in those articles, Dr. Moeckel, would you agree that even clinically detectable AKI may not cause permanent injury where normal repair mechanisms keep pace with the injury resulting in functional resolution?

MR. PENNOCK: Objection.

A I think that cannot be categorically said as such. You know, the progression of AKI to CKD is very much dependent on the individual patient, and we now know that possibly also genetic factors might be underlying the

progression from AKI to CKD. So regenerative cell activity alone per se may not be enough.

So I think, you know, the question cannot be answered just categorically in that way.

BY MS. ALTHOFF:

Q Doctor, the studies that -- that you -- not studies -- the papers that you talked and cited, the Basile paper, the Venkatachalam paper, and the Zuk paper, those are all, like, review articles; correct? As opposed to individual studies, for example?

A Yeah. Several of the studies that I quote here are review articles. That's correct.

Q Uh-huh.

And do those review articles give sort of a summary or overview of animal studies using animal models of AKI?

A Yes, I believe so.

Q And I think you mentioned early on in the deposition that you, yourself, are familiar with animal models of AKI, including the ischemic reperfusion model and even some drug-induced models like cisplatin; correct?

A Yes.

Q Were you aware that PPIs have been

shown to be protective against AKI from renal ischemic reperfusion injury in rats?

MR. PENNOCK: Objection.

A I believe I have seen such a study, yes.

BY MS. ALTHOFF:

Q And are you aware that PPIs have attenuated cisplatin-induced kidney injury in rats?

MR. PENNOCK: Sorry. Can you repeat that, please?

MS. ALTHOFF: Sure.

BY MS. ALTHOFF:

Q Are you aware of whether PPIs have been found to attenuate cisplatin-induced kidney injury in rats?

MR. PENNOCK: Objection.

A No, I'm not aware of that.

MS. ALTHOFF: Let's pull up my 32 as Exhibit 9, please.

(Whereupon, Exhibit No. 9, "Omeprazole attenuates cisplatin-induced kidney injury through suppression of the TLR4/NF-?B/NLRP3 signaling

pathway," was marked for identification.)

BY MS. ALTHOFF:

Q Doctor, I'm handing you what's been marked as Exhibit 9, is a piece of medical literature entitled "Omeprazole attenuates cisplatin-induced kidney injury through suppression of the TLR4/NF" -- and a bunch of other letters -- "signaling pathway." This appears to be an article published in Toxicology in 2020 by first author Gao.

Is this a piece of literature that you recall having reviewed prior to today?

A Let me quickly put -- pull this up.

Q Sure.

A Yes. I -- I believe that I have seen this paper before.

Q Okay. And it -- it's -- it's a recent 2020 study; correct?

A Correct. Yes.

Q And did this study find -- or an indication that, at least in rats, omeprazole inhibited cisplatin-induced kidney injury?

A Yes. It -- that study apparently shows that omeprazole is ameliorating cisplatin-mediated

kidney injury. That's true.

Q This is not a study that you relied on in reaching your opinions in this case; correct?

A No, it wasn't, because this is a completely different approach and mechanism.

Basically, what the authors are trying to do is to see the effect of omeprazole on cisplatin-induced inflammatory injury and apparently to -- according to the results, there is a inhibitory effect on the inflammatory mechanism that underlies cisplatin-induced kidney injury.

That -- this is a study that, in my opinion, does not prove that proton-pump inhibitors are beneficial and preventive of AKI.

The only thing that they show in this one single animal model was that omeprazole had a, apparently, beneficial effect on an inflammatory reaction that is associated with cisplatin toxicity in this model.

I was asked to review what the effect is on -- of proton-pump inhibitors directly in -- in different animals, which is a completely different experimental situation. So I did not think that this paper had any important additional

information to the questions I was asked to review and answer.

Q Right.

So the cisplatin injury is a model of AKI; correct?

A Yes.

Q And similar to the IR or ischemic reperfusion model in rats is a model for AKI; correct?

A Yes. Although I want to just point out that ischemic reperfusion as an AKI model is very much on a molecular basis completely different from cisplatin-mediated acute kidney injury.

Q Which of these models, if either, do you think is similar to your opinion that PPIs cause acute injury in -- at least in animals?

A So from my opinion, when I look at the pathology that PPIs induce in mice, rats, and dogs, I would say that ischemia reperfusion would be a type of injury model that would be along the pathways of PPI-mediated tubular injury.

Q And I think you told us just a few minutes ago that you were aware that PPIs have been found, at least in rats, to have a protective effect when pretreated against renal ischemia

reperfusion injury in rats?

MR. PENNOCK: Objection.

A I did not say that. I said I am aware of an article like that, but it doesn't mean that I concur.

BY MS. ALTHOFF:

Q Okay. Maybe I misspoke.

I was asking -- that's what I meant to ask you, was whether you were aware of any studies to that regard?

A I'm aware that the study exists, and that's -- was my answer. I'm aware. But I concur -- I don't concur.

Q Okay. And, you know, why, Dr. Moeckel, do you not concur that PPIs in that study were shown to have a protective effect against renal ischemia reperfusion injury in rats?

A I think we need to pull up that study and look at it.

Q Sure.

MS. ALTHOFF: Let's look at my 30, which will be Exhibit -- I think it's 10.

(Whereupon, Exhibit No. 10, "The protective effect of acute

pantoprazole pretreatment on renal ischemia reperfusion injury in rats," was marked for identification.)

BY MS. ALTHOFF:

Q Handing you what's been marked as Exhibit 10. This is a study entitled "The protective effect of acute pantoprazole pretreatment on renal ischemia reperfusion injury in rats," the first author Kohansal, in the Fundamental & Clinical Pharmacology 2019.

Do you see that?

A Yes. Let me download the article and quickly look at it, please?

Q Uh-huh.

Have you had time to refamiliarize yourself with this --

A Yeah.

Q -- study?

A I -- I -- yeah. I now remember reading this study sometime ago.

And the reason why I was not very impressed with this study is, first of all, that I think the tubular injury that they report is not that significantly increased compared to the

normal tissue control. Moreover, as a mechanism, they describe the inhibitory effect on the Toll-like receptor 4.

And when I look at the graphs, Figure 5 in that paper, I did not think that the pantoprazole effect on the Toll-like receptor was that impressive.

You know, you're welcome to look at Figure 5 in that paper, and you can see that the Toll-like receptor 4 even was increased in pantoprazole. That's not really decreased very much. They say, you know, it's statistically significant, but looking at this, that is not very impressive at all.

So I don't -- I don't believe -- if I were a reviewer, I would reject this paper. This is -- does not look like a very impressive effect. It is very modest. The histology is not convincing. I -- I would have never approved the publication of this paper. So I am not very impressed by these results.

Also, tubular cell injury has many mechanisms, many kind of cell death that happens: Organized necrosis, ferroptosis plays a big role, pyroptosis. It's not what they claim a

apoptosis-associated mechanism.

So I do not think that this paper is particularly relevant.

Q Would you agree, Doctor, that the difference between the -- the sort of effect size between the control group and the drug group, if -- if it's not a significant difference -- and by "significant," I mean a large difference -- that that affects the quality of the study?

A Yes. As you can see in Figure 5, only the 36-milligram per kg pantoprazole concentration is apparently statistically significant. You know, I -- I -- I -- I wonder whether that is true or not, you know.

And you can see that compared to the sham controls, the effect by pantoprazole on the Toll-like receptor, for instance, and also on the kidney histology and the oxidative stress.

So all of these effects are incredibly modest.

Q Uh-huh.

A So in other words, if I had been a reviewer on this study, I would not have believed these results, and I certainly would not have approved the publication of this study.

Q Are you able to tell from looking at Figure 5 what percentage difference there is between the -- sort of the lowest pantoprazole group and the control?

A Well, it's -- I -- I think that's only, you know, a very modest decrease. I -- I would have to guess. If you said, you know, percentage, I -- I think that could be only guesswork in -- in the way the data is displayed.

Q Would you consider a 20 percent change to be a modest change?

A First of all, I don't think it's -- it's as much as 20 percent. And -- and -- and a 20 -- 20 percent change, in my opinion, yes, would be a -- a modest change.

Q Uh-huh.

A So in -- in other words, I -- I think the apparent protective signal that the authors claimed to see in this study is believable or acceptable in my opinion. I think the -- the results are not very convincing.

Q And that's primarily because of the modest effect, at best, seen between the controls and the pantoprazole-treated groups?

A Yeah. And --

MR. PENNOCK: Objection.

A And -- and especially, you know, the effect is only seen in the 36 milligrams, so in the highest group. And the effect also doesn't show any kind of, like, dose dependency. So I think that the results are not very convincing.

BY MS. ALTHOFF:

Q And, of course, dose dependency is a very important aspect when looking at toxicologic studies as well; correct?

A Yeah. Especially, if you want to show that the protective effect by the drug is really through a specific mechanism.

So we all know if the drug inhibits a activity center in an enzyme, for instance, that regulates cell death, then you would expect to see dose dependency and that effect and, therefore, argue this specific mechanism -- this protective effect that apparently is seen in this one high-dose group is so small that I -- I even wonder whether that could be somewhat random.

Q And again, not only in studies were they're looking at drugs having a protective effect, but also drugs having any kind of adverse effect on animals' dose dependency is a

significant finding; correct?

MR. PENNOCK: Objection.

A To be honest with you, you know, if -- if I see in a study that a certain type of injury is exacerbated with increase in dosage, that makes me very worried. I think that is an important signal that needs to be further investigated.

BY MS. ALTHOFF:

Q And conversely, lack of dose dependence would also be an important factor for you in looking at toxicologic findings --

MR. PENNOCK: Objection.

BY MS. ALTHOFF:

Q -- in animal studies?

MR. PENNOCK: Objection.

Incomplete hypothetical.

A So I would not necessarily say that if there's absence of dose dependency in injury, that the injury does not happen. But certainly, if you can see dose-dependent increase in injury, I think that is an important finding that should be further investigated.

BY MS. ALTHOFF:

Q All right. Let's go back to your report and specifically your discussion of the

AstraZeneca preclinical studies or nonclinical studies. So starting on page 7.

And I think we discussed already that, as part of your review, you reviewed the study reports for these particular studies that you included in your report and then for the ones in the report, as well as in Appendix A you reviewed slides; correct?

A Yes.

Q And, I mean, is it your understanding that the study reports that you reviewed had been submitted to the FDA as part of the drug approval for the medications that were studied in those reports?

A Correct.

Q With regard to the study on page 12 -- we'll start with the one on page 12 and 13 of your report, which is T 7 -- 1371, "General Toxicity in Dogs of Omeprazole Given Orally by Gastric Tube for One Year."

Do you see that?

A Yes.

Q And you identified three animals in particular, animal 1922, animal 1936, and animal 1941. And these were B, C, and D in your pictures

right above that section.

A Correct.

Q Okay. And with regard to animals 1922 and 1941, you identified tubular vacuolization on those animals; correct?

A Correct.

Q And as you sit here today, do you know whether tubular vacuolization was reported for those animals by AstraZeneca in the study report?

A So again, I would need to rely on my memory. And I am not certain, but I know that in several studies, AstraZeneca did report vacuolizations. So I assume it probably was mentioned in the report.

Q Sorry. You assumed what?

A That vacuolization was mentioned in their report.

Q Okay. With -- and so this particular study, 1371, was in -- as we said, was in dogs; right?

A Sorry. Sorry. It's 1371?

Q Yes. The one we've just been talking about. Same study, Beagle dogs.

A One moment, please.

Q Sure.

Page 12 of your report.

A Yes.

Yes. 1371 is a long-term study in Beagle dog.

Q Uh-huh.

Do you agree, Dr. Moeckel, that 50 -- 50 to 60 percent of Beagle dogs in standard toxicology studies exhibit histologic findings in the kidney?

A Sorry. Again, there was an acoustic problem. Can you repeat the question one more time, please?

Q Sure. Make sure I get it right here.

Would you agree, Dr. Moeckel, that 50 to 60 percent of Beagle dogs in standard toxicology studies exhibit histologic findings in the kidney?

A I tend to not agree. That's at least not pathological lesions. I -- I have probably looked at more rat and mice kidneys. I have looked at some dog kidneys. And my experience across animal species is that a normal, healthy kidney looks pretty much the same in any mammal and -- including humans.

So I -- I would be surprised if that

actually would be true, that 60 percent of Beagle dogs show histopathological abnormalities.

I'm sorry, but I -- this is very hard for me to believe.

Q And do you know whether the most common histologic findings in Beagle dogs in toxicology studies are mineral deposits, interstitial mononuclear cell infiltrates, focal pigment deposition, and chronic interstitial nephritis?

A I'm not aware of that.

Q All right. So back to our two animals in 1371, the dogs that you identified tubular vacuolizations, so that being animal 1922 and 1941, if I'm --

A Yes.

Q -- getting this right. Yes.

Doctor, would you agree that the finding of tubular vacuolization is often due to autolysis due to the time between sacrifice and fiction -- fixation?

A No. I strongly disagree.

Q Do you know how much time typically occurs in a toxicology study between the time that a dog is sacrificed and when its kidneys are harvested for review?

A I would say within 60 minutes the kidneys should be harvested and put in formalin at the latest.

Q Are you aware that kidneys are one of the last organs --

(Whereupon, the court reporter requests clarification.)

A And -- and put in formalin for fixation.

COURT REPORTER: My apologies.

BY MS. ALTHOFF:

Q Would you agree that kidneys are typically the last organs that are removed at necropsy?

A I disagree.

Q Dr. Moeckel, in your opinion, how much time would have to elapse between sacrifice and fixation before autolysis could cause tubular vacuolization artifact in a Beagle dog?

A Can you repeat the question one more time, please?

Q Sure.

Dr. Moeckel, in your opinion, how much time would have to elapse between sacrifice and fixation before autolysis could have caused

tubular vacuolization as an artifact in a Beagle dog?

A I would say that the kidney should be fixated within 30 to 60 minutes, at -- at the latest, to prevent artifact to develop.

Q With regard to animal 1936 where you identified tubular pigmentation, that was a single male animal; correct?

A Yes.

Q And you didn't see tubular pigmentation in other animals in this study?

MR. PENNOCK: Objection.

A I believe that in this particular animal, the pigmentation was very pronounced. That's why I pointed it out in the image.

I believe that there was also milder form of pigmentation in the animal in picture C -- sorry -- the animal in picture D, the female, at 80.

BY MS. ALTHOFF:

Q Would you agree, Doctor, that tubular pigmentation is typically related to vasculitis that is commonly seen in Beagle dogs?

A No. I disagree with that.

Q All right. Let's look at page 17 and

18. This is another dog study, T2237, three-month omeprazole.

Do you have that, Doctor?

A Would you repeat the number one more time, please?

Q Sure. It's T2237. It's on page 17 of your report.

A Yes.

Okay. I have it.

Q And in that study, again, you identified some animals on the next page, I believe, 2167 and 2188. And those are pictures B and D in your depiction?

A Yes. That's correct.

Q And for both of those animals, you identified them as having cytoplasmic vacuolization; correct?

A Cytoplasmic vacuolization, I have it for animal A and B.

Q Yes. 2167 and 2188; correct?

A Correct.

Q And is cytoplastic vacuolization another term for the same finding that you saw in the prior animal that we just talked about, which was called tubular vacuolization?

A Yes. It's the same entity.

Q And once again, do you disagree that those findings of cytoplastic vacuolization in animals 2167 and 2188 could be due to autolysis?

A Yes.

And I would like to explain why, because when you see autolysis, you do not see isolated cytoplasmic vacuoles in an intact cell.

Autolysis is defined by tubular necrosis, which is defined by tubular cells falling apart, sloughing off the basement membrane, and not showing the cell borders and integrity anymore.

So to use the word "autolysis" and "vacuolization" in the same term is flawed because vacuolization is not a feature of autolysis or the features of autolysis are cells breaking up, losing brush border, losing their cytoplasmic borders, basically the image of what we call coagulative necrosis.

Q Looking at pages 21 to 22 of your report, once again a dog study, this time a three-month esomeprazole neonatal dog study, 900186?

A Uh-huh.

Q Do you have that?
A One moment, please.
Q Sure.
A Could you repeat the number one more time?
Q Uh-huh.
Page 21 to 22 of your report, Study 900186 --
A Yes, I have.
Q -- a three-month study in neonatal dogs with esomeprazole.
A Yes, I have it.
Q And once again, you've -- you have identified animals 301 and 353?
A One moment.
Yes, that's correct.
Q And for the -- the female from group 3, you've identified brush border loss and vacuoles.
Do you see that?
A Yes.
Q And is that, again, a reference to tubular vacuoles or cytoplasmic vacuolization?
A Yes. But brush border loss is also a reference to acute tubular necrosis.
Q And so with the group 3 female, are you

able to rule out autolysis?

A Can you repeat this? I -- you broke up.

Q Yeah. Sure.

So with regard to the group 3 female who you identify as having brush border loss and vacuoles, are you able to rule out autolysis in that sample?

A Yes, I believe I can rule out autolysis, because autolysis shows widespread necrosis of tubular epithelium.

Q So then if we go to pages 10 and 11 of your report, again starting at the bottom of page 10, Study T 1932, this is a seven-year dog study, but this is the three-year interim report; correct?

A Correct.

Q And once again, we've identified animal No. 10 as having vacuolization; correct?

A Correct.

Q And so, you know, despite, you know, whether, you know, you've called it a vacuole or cytoplasmic vacuole or vacuolization, those are the same findings in each of those animals that we've just gone through in those dog studies; is

that correct?

A Yes. That's correct.

THE VIDEOGRAPHER: Doctor, if you could tilt your screen down just a little bit for me, please? Thank you.

COURT REPORTER: Jeff, can you make it bigger? It's very small, the -- the text on this one.

MS. ALTHOFF: Are we good?

THE WITNESS: Yes. It's better.

BY MS. ALTHOFF:

Q Going back to that first study -- dog study we talked about, which was T 1371, dogs given omeprazole for one year. It's on pages 12 and 13 of your report, Doctor.

A T 1371; correct?

Q Yes.

A Okay.

Q And you identified nephrocalcinosis, among the other findings, in the dosed animals?

A I believe the investigators found nephrocalcinosis.

Q Thank you for clarifying that. That was really sort of my question.

Did you identify nephrocalcinosis in

any of the animals that you saw?

A Yes, I did.

Q Okay. Are any of those depicted on page 13?

A No, they are not.

Q Okay. So AstraZeneca reported minimal degree nephrocalcinosis, and you also saw nephrocalcinosis in some of the samples that you saw?

A Yes. Correct.

Q Was the nephrocalcinosis that you saw in Study T 1371 dystropic or metastatic?

A Dystropic.

Q Would you agree that dystropic nephrocalcinosis occurs spontaneously in laboratory animals?

A It may occur spontaneously in some laboratory animals.

Q Do those laboratory animals include Beagle dogs?

A I believe it's described in Beagle dogs, but I do not have enough experience myself with Beagle dog kidneys to confirm that from my own experience.

Q And from looking at the slides on T

1371, do you know whether these were Beagle dogs or some other strain?

A I know that they were Beagle dogs, yes.

MS. ALTHOFF: All right. Let's look at my exhibit that shows Exhibit -- Appendix A. So let's go to the next page.

BY MS. ALTHOFF:

Q And in this --

MS. ALTHOFF: Actually, go back one page. Thank you.

BY MS. ALTHOFF:

Q -- you discuss the rest of the dog studies that you received slides on that you reviewed; correct?

A Correct.

Q And you list four, five, six -- if I'm counting these right, six studies of three months on dogs; correct?

A Correct. Yes.

Q Uh-huh.

And once again, on these dogs you saw the same type of vacuoles that you saw in those other dog studies that you reviewed?

A Yes, that's correct.

Q And were you able to rule out autolysis in these studies as the cause of the vacuoles?

A Yes. There are -- was no evidence of autolysis in my opinion.

Q And same sort of question for your -- the short-term, less-than-one-month dog study that you looked at, which is B-1396, a two-week omeprazole pilot study on the next page.

Do you see that?

And once again, you identified having seen this again, the same type of vacuoles identified previously in the other studies?

A Yes. Similar type of vacuoles, but I did not see evidence of autolysis.

Q Okay. And I think you told us already that it was your understanding that the study reports that you reviewed had been submitted to the FDA; correct?

A Correct.

Q And, in fact, you quote from some of the study reports directly in the body of your report in sections that you have put into quotation -- with quotation marks; correct?

A Can you show me specific examples that you are --

Q Sure.
A -- referring to?
Q Yeah.
So let's look at page 9, for instance, of your report.
A Uh-huh.
Okay.
Q And if you look at the first sentence, it says, "In the body of the study reports I reviewed, these separate lesions are characterized" -- and then in quotation marks, it says -- "'glomerulonephritis or chronic progressive renal disease (nephropathy).'"
A Yes.
Q Do you see that?
A I see that.
Q And is that an actual quote from the AstraZeneca reports?
A Yes.
Q And some of the quoted language in your report includes a discussion by AstraZeneca in the report of exacerbation of chronic progressive nephropathy in the treated or dosed groups; correct?
A Where is that, please? Can you point

me to that?

Q I'm missing my page cite for this one.

Well, let me ask you this question: Do you recall reading, in any of the study reports on rodents that you reviewed from AstraZeneca, the reference in the report to exacerbation in the dosed groups of treated animals?

A Yes. I remember reading in the AstraZeneca report of one study, at least, that they noticed a exacerbation of the pathology by increased dosage of the drug.

Q Right.

And as I recall now, that was one of the criteria that you used in determining which studies to ask for slides from, was if that information was included in the report?

A That is true.

Q Are you aware of any concerns raised by FDA in response to any of the kidney findings identified in AstraZeneca's preclinical study reports that you have included in your expert report?

MR. PENNOCK: Objection.

A Can you repeat the question one more time, please?

BY MS. ALTHOFF:

Q Sure.

Are you aware of any concerns raised by FDA in response to any of the kidney findings identified in AstraZeneca's preclinical study reports that you have also included in your expert report?

MR. PENNOCK: Objection. Form. Beyond the scope. Foundation.

A I'm -- no, I'm not aware.

BY MS. ALTHOFF:

Q I'm going to want to go through the rat studies like we did just with the dog studies here in your report, and so we're going to be talking about basophilia and casts and those types of observations again that you made in the slides that you reviewed.

And so is it a -- well, let me ask you this: Did you see chronic progressive nephropathy or something you would identify as chronic progressive nephropathy in any of the studies from AstraZeneca that you reviewed?

A No.

Q Would you agree that -- well, when did you first learn about chronic progressive

nephropathy? Do you recall?

A I -- I have been aware for a while about chronic progressive nephropathy for many years that this is something that is known in rats, and it's a lesion that occurs in older rats and can be dependent apparently on the rat chows or, I believe, high protein and high fat rat chow can contribute to chronic progressive nephropathy. So I've been aware of that for many years.

Q Have you ever had the occasion previously to determine whether animals showed signs of chronic progressive nephropathy in other toxicology studies that you've done?

A So I've conducted quite a lot of rat and mouse kidney histologically evaluations for a large number of different types of kidney injury models, including also toxicology studies.

And I have looked at hundreds and hundreds and hundreds of rat and mouse kidney sections, and I have never in rats that I have studied seen chronic progressive nephropathy. Those animals --

Q And you didn't see it here either; correct?

MR. PENNOCK: Objection.

You -- and you interrupted the witness.

A So as I said, I -- I have never seen chronic progressive nephropathy in any of the hundreds of rats that I have examined histologically.

BY MS. ALTHOFF:

Q And I think you told us earlier that you haven't conducted any toxicologic studies on rats for more than, like, a year; correct?

A Correct. Yes.

Q And since in your opinion chronic progressive nephropathy doesn't start until 18 months, from your perspective you shouldn't be seeing chronic progressive nephropathy in any of your studies as a normal finding; correct?

A Correct.

Q So again, you disagree that lesions consistent with chronic progressive nephropathy can be seen in rats as early as two months of age?

A Yes. I disagree completely.

Q Do you agree that it requires a finding of thickening of the tubule basement membrane, casts, and basophilia?

A Can you please repeat the question?

You broke up.

Q Sure.

Do you agree that chronic progressive nephropathy as a diagnosis requires a finding of thickening of the tubule basement membrane, casts, and basophilia?

A Yes, I agree.

Q Do you agree that it's recommended that toxicologic pathologists recognize the complex as a single entity, that being CPN, rather than listing the individual components such as basophilia when reviewing past --

A I disagree.

Q -- slides?

A I -- I disagree. I think -- I think that tubular basophilia can be a feature due to many other things aside from CPN and, therefore, tubular basophilia should be mentioned in toxicology experiments when it's seen, especially if it's dose-dependent.

Q And would you have the same answer if the tubular basophilia was in combination with the other two items identified, that being casts and thickening of the tubule basement membrane?

A I think it -- in -- in the situation

that you have basophilia with tubular basement membrane thickening, I would say you may use the term "CPN."

Q Okay. Okay. Let's look at page 13 through 16 of your report, and this involves Study T 1347, rats given omeprazole for six months?

A Yes.

Q And in this study, you identified tubular injury with casts, tubular injury with nuclear drop-out, and sloughing of tubular cells, casts, and basophilia; correct?

A Yeah. So what I found was tubular injury, casts, nuclear drop-out, and sloughing of tubular epithelial cells, yes.

Q Okay. And you also found basophilia?

A Yes, I did.

Q Each of those types of components has been associated with the nomenclature of chronic progressive nephropathy; right?

A No. That is not correct.

Q Why is it that you have determined that these findings in this six-month omeprazole rat study are not chronic progressive nephropathy?

A Because, as shown in image D on page 14, I described tubular injury was nuclear

drop-out and sloughing of tubular epithelial cells, which are not features of CPN.

Q Okay. Tubular injury with casts, is that a feature of CPN?

A Tubular injury with nuclear drop-out and sloughing of tubular epithelial cells and sloughing of the brush border is an acute lesion and is not a part of CPN, no.

Q Okay. I'm -- I'm asking you now about the -- the picture that's C, which did not have the nuclear drop-out and sloughing. It just says, "Tubular injury with casts."

And my question is: Is tubular injury with casts consistent with CPN?

A So what I mean on the tubular injury in the context of all of these images entails nuclear drop-out and sloughing of tubular epithelial cells. So what I'm referring to is acute tubular injury.

I may have described that a little bit too general. So in all of these images, what we are seeing is acute tubular injury that entails, as a definition, nuclear drop-out, sloughing of tubular epithelial cells, brush border sloughing, the classic findings of acute tubular injury. And

that is not part of CPN.

Q Okay. Looking at page 15, the second one down there with the big yellow arrow, this is, again, still a animal from T 1347; correct?

A Correct.

Q So six months' omeprazole rat.

And you identify casts and basophilia, but you do not identify tubular injury for that one; correct?

A No. That's not correct.

I pointed out, in addition to the previously described lesion, basophilia and casts. But all of these images that I show from the study show acute tubular injury.

I did not repeat that in each of these images, but all of the kidney lesions that I found and described and took pictures of showed acute tubular injury with sloughing of tubular epithelial cells, nuclear drop-out, and loss of the brush border.

And in addition, in these images of -- on page 15, I saw casts and extensive basophilia, and I just pointed that out in addition to the tubular injury.

These are all acute tubular injury

lesions that you are seeing here in these images.

Q Okay. So we can go through all of these studies, Dr. Moeckel, but my understanding now from your discussion is that you don't believe you saw chronic progressive nephropathy in any of the studies regardless of -- any of the rat studies, regardless of how long they were conducted; is that correct?

A Yes.

Q So when you said things like basophilia, casts, etc., you don't consider those to be components of chronic progressive nephropathy, but they're components of a different acute tubular injury that you've identified?

MR. PENNOCK: Objection to form.

Go ahead.

A That is correct.

BY MS. ALTHOFF:

Q Let's look at just one more -- so actually, on Appendix A, if we can go back to that, which is, again, the studies that didn't -- aren't in the sort of main part of your report, but they are ones where you looked at the slides.

And if you look at the three-month rat study at the top, which is 96153 -- we talked

about this briefly earlier -- you identified calcium crystal precipitations, among other signs, but --

A Yes. I did, yes.

Q Would you agree that it's been long understood that renal mineralization is a ubiquitous lesion found in chronic rat studies?

A I think that is way too general to put it that way, in my opinion.

Q The calcium crystal precipitation that you identified in this study, is that a form of renal mineralization?

A No.

So when you look at -- when you talk about calcium crystal in the kidney, there are different lesions that you have to distinguish.

You have to distinguish between a calcium oxalate or calcium phosphate crystal that precipitates in the tubular lumen or in the tubular epithelial cell, and you have to distinguish about -- distinguish those crystals from calcium crystals that develop on a atrophic nidus leading to what is called dystrophic calcification. And biochemically, those are totally different things.

So the calcium crystal precipitation in this animal in -- in -- in this rat study is indicative of some kind of pathological process that is associated with the proton-pump inhibitor, and it's not random.

Q Do you know how many animals in the three-month rat study, 96153, had calcium crystal precipitations as you've identified?

A So I -- so I -- I remember seeing several animals. I don't know the exact number off the top of my head, but I can certainly provide that number to you.

Q And how is it that you were able to determine that the crystal -- calcium crystal precipitations were due to the omeprazole portion of the combination product as opposed to the amoxicillin or the fungicide?

A So the -- the way the calcium crystal precipitation happened was along the tubular injury, and I only saw it in those animals that were also receiving the omeprazole because they were control animals that did not receive the omeprazoles.

And I saw these findings, the crystals, only in those animals that had the omeprazole and

not in the control animals.

Q Did the control animals in 96153 receive the other two parts of the combination?

A I believe so, yes.

Q Did you see calcium crystal precipitation in any of the other rat studies -- the AstraZeneca preclinical rat studies where you reviewed the slides?

A Yes, I did.

Q And I don't recall having seen that in any of the other studies that you've discussed in your report.

Do you have a recollection of which studies you saw that?

A So I saw it in the rat studies that were one month or less. So those are also in the Appendix A, the 900, 404, and the T 1441.

Q Is that the reference to calcification?

A Yes.

Q If you look at page 20 and 21 of your report, bottom of page 20 starts with your analysis of a one-year neonatal rat study, T2793, with omeprazole.

Do you see that?

A Yes, I see that.

Q And did you identify any mineralization or -- or calcium crystallization in that study?

A Not that I remember.

Q Oh, sorry. I thought -- thought you were going on. Thank you.

Specifically looking at animal No. 5862 from that study, which I think is your B.

A Uh-huh.

Q Is -- is that animal B, 5862?

Yeah, I believe it is.

A Yeah.

Q Yes?

A Yeah. Uh-huh.

Q Okay. In reviewing the AstraZeneca clinical study -- preclinical study report related to Study T2793, did you identify animal 5862 as being renal hypoplastic?

A Sorry. You broke up. Can you repeat that one more time, please?

Q Sure. I'll read it back so I don't have to remember it.

In reviewing the AstraZeneca clinical -- preclinical study report related to Study T2793, did you identify animal 5862 as being renal hypoplastic?

A No.
Q Are you familiar with the condition of renal hypoplasia in rats?
A Yes.
Q Are you aware that renal hypoplasia can cause all kinds of abnormalities in rats with that condition?
MR. PENNOCK: Objection.
A So renal hypoplasia is a lesion where the nephrons are not fully developed, and there are a number of features that you see, but they should not be necessarily confused with toxic injury lesions.
BY MS. ALTHOFF:
Q Right.
The renal hypoplasia or hypoplastic lesions look different and should not be confused with pathologic lesions; correct?
A Yes. With toxic -- with toxic pathologic lesions.
Q You mentioned early on that when you were doing your work that ultimately became the report, which is exhibit -- well, your report exhibit, that you had images that you put into a PowerPoint, and then you created certain footnotes

relating to those images; is that correct?

A Yes.

Q Is there a separate PowerPoint that relates to your report which contains images from the AstraZeneca preclinical studies?

A No.

Q What happened to the PowerPoint that you created?

A Oh, you mean the -- the PowerPoint of the respective image that I have in my -- in my report?

Q Yes.

A Yeah. I -- I still have that.

Q Does the PowerPoint contain any information that is not included in your report?

A No.

Q Does it contain any images other than the ones depicted in your report?

A No.

Q Does it contain any histopathologic findings or observations other than what are contained in your report?

A No.

MS. ALTHOFF: Let's take just a couple-minute break. I want to make

sure I'm -- see what I have left.

MR. PENNOCK: Well, hold on a second. Do you -- do you have a lot left or a little bit?

MS. ALTHOFF: I probably have an hour, is my guess, but I just want to make sure I haven't missed a whole section somewhere, 'cause I kind of jumped around from what I had planned.

MR. PENNOCK: If it's all right with you, let's go till five o'clock, and then take a break.

MS. ALTHOFF: Okay. We can do that.

MR. PENNOCK: Is that all right?

MS. ALTHOFF: Do you want to go a little longer?

MR. PENNOCK: Unless you -- I just think, push till 5:00, and then you could take your break, and you'll have an hour to wrap up.

MS. ALTHOFF: Okay. And it --

MR. PENNOCK: Is that all right?

MS. ALTHOFF: Yeah. I mean, you guys are out of there at 6:30. So I

assume you don't want to start Takada today.

MR. PENNOCK: Not unless we have time left. But anyway, let's -- let's just go ahead and --

MS. ALTHOFF: Okay.

MR. PENNOCK: -- just get -- you get down, you'll have an hour left. We'll take a break. You can, you know, see what you want to do.

MS. ALTHOFF: So --

MR. MIZGALA: Just with respect to -- to me, I think when Katherine is done, we want to take a break, because she's covered a lot of what I already have in my outline.

MR. PENNOCK: Sure.

MR. MIZGALA: So I would, like, prefer having overnight to go through and slicing all that out.

MR. PENNOCK: Yeah. I'm not going to -- I'm not going to force you to -- to go forward. That -- that's fine.

MR. MIZGALA: Okay.

MR. PENNOCK: I don't know if I

could, but I don't know how I would do that.

MR. MIZGALA: You're such a -- you're such a gem, Paul.

MR. PENNOCK: If I could figure it out, I'll force you.

Okay. So let's go to 5:00, and then that'll give you an hour if you still have to; all right? So I'll agree to that.

MR. MIZGALA: Uh-huh.

BY MS. ALTHOFF:

Q Okay. Looking at --

MS. ALTHOFF: I'm sorry. Are we back on, Jeff?

BY MS. ALTHOFF:

Q Okay. Let's look at Appendix B to your report, which I don't think we've looked previously as a stand-alone exhibit.

MS. ALTHOFF: If -- if we haven't, let's make this as a separate exhibit. It's my 4.

THE VIDEOGRAPHER: This will be 11.

(Whereupon, Exhibit No. 11, Appendix B, AZ Studies: Renal Slides Requested but Not Received, was marked for identification.)

MS. ALTHOFF: Okay. Great.

BY MS. ALTHOFF:

Q Showing you what's been marked as Exhibit 11 to your deposition, Dr. Moeckel, is this a document that you put together summarizing AstraZeneca preclinical studies for which you did not review slides?

A Yes.

Q And I mean, you would agree, Dr. Moeckel, that this is a subset of the full available studies out there with regard to omeprazole or esomeprazole in animals --

A Yes.

Q -- done by AstraZeneca?

A Yes.

Q And with regard to these particular studies on -- on these pages of Exhibit B, you were quoting from or summarizing from the actual study reports that were submitted to the FDA relating to these studies; correct?

A Correct.

Q And to the extent there's information that's in quotation marks, that would be a verbatim quote from those studies; correct?
A Yes.
Q So if we look at page, I think it's five -- they're not numbered, but I think it's page five of Exhibit B to your report -- that's it -- and you look at SR 9827201.
Do you see that? The study title?
A SR 98272 -- 27201. Yup.
Q And this is a 13-week study in Sprague-Dawley rats looking at omeprazole and esomeprazole?
A Yes.
Q And in this particular study, would you agree that the AstraZeneca investigator reported renal basophilia in all groups, including controls, but increased in incidence and severity with the dose?
A Let me quickly review.
Q Uh-huh.
MR. PENNOCK: Note my objection to the question.
A Yes. I agree.

BY MS. ALTHOFF:

Q So in this study, the 13-week study -- so it's less than an 18-month-old rat; correct?

A Yeah. I'm -- I -- so -- so, yeah.

Those rats are younger than 18 months old, yes.

Q And AstraZeneca reported in its preclinical study report to the FDA that they had seen exacerbation of chronic progressive nephropathy in the dosed groups; correct?

MR. PENNOCK: Note -- note my objection to form and foundation.

BY MS. ALTHOFF:

Q You can still answer, Dr. Moeckel.

My question is: Did AstraZeneca put in the -- the report that you reviewed that they had seen an exacerbation of chronic -- chronic progressive nephropathy in the dosed groups?

A Yes. They see an exacerbation in the chronic dosed group.

Q And it was seen in both sexes, male and female; correct?

A Yes.

I also want to say on record that they describe tubular basophilia as being a sign of

chronic progressive nephropathy, and I disagree with that statement.

Q You disagree that tubular basophilia can be associated with chronic progressive nephropathy?

A No. I -- I disagree with the sentence that they said tubular basophilia is a sign of chronic progressive nephropathy, because tubular basophilia alone should not be interpreted as a sign of chronic progressive nephropathy.

Q And so from your perspective -- again, this is a 13-week study. So these would be not particularly -- would not be 18-month-old rats.

So, therefore, you could not diagnose them with chronic progressive nephropathy based on tubular basophilia alone?

A Well, and in addition there are not these important other findings of chronic progressive nephropathy, which are thickening of the tubular basement membrane, thickening of the glomerular basement membrane, and glomerulosclerosis.

Q And from your perspective, you have to see all three of those, even in a 13-week study, in order to characterize it as chronic progressive

nephropathy, whether that's even early stage?

A Yes, that's correct.

Q All right.

MS. ALTHOFF: How -- did you say we were going to go till 5:30? Is that what you said, Paul?

MR. PENNOCK: Well, no. I mean, we can take a break at 5:00. How about that?

MS. ALTHOFF: Well, I'm getting ready to change a topic. So let's take a break now. And then we might even be done by 5:15.

MR. PENNOCK: Okay. Let's -- let's -- let's do that.

MS. ALTHOFF: Okay. Let's take five -- five minutes or so.

THE VIDEOGRAPHER: Off record 4:47 p.m.

(Whereupon, there was a recess taken from 4:47 p.m. to 5:00 p.m.)

THE VIDEOGRAPHER: On the record 5 p.m.

BY MS. ALTHOFF:

Q And, Doctor, we're back from another

brief break.

I realized I don't think I asked you this question, but -- so all of the studies that you reviewed, the AstraZeneca preclinical studies where you saw lesions on the slides, those were animals that had been treated with PPIs; correct?

A Correct.

Q And so did you see similar lesions, for instance, in the control groups?

A Not to my recollection, no. The control group animals, most that I reviewed did not show significant lesions.

Q And did you see lesions in any slides of animals that were dosed with something other than a proton-pump inhibitor?

A No. I don't have any recollection of that.

Q Okay. So I want to go back to sort of where we started here at the beginning, and I think you told us -- hold on -- that you were retained by plaintiff's counsel in spring or summer of 2018; correct?

A Correct. Yes.

Q And you were retained at, I think you said, $400 an hour; right?

A Correct. Yes.

Q Okay. Now, prior to that, you were retained by my office in this litigation; is that right?

A I don't collect [sic] being retained. I coll- -- I -- I remember that I had a conversation with one representative from your office, but I do not remember being retained.

I do not remember that I received any payment. I do not remember that I signed any contract with you.

Q When you say somebody from my office, it was actually me, wasn't it?

A I apologize if I did not recognize you. It -- it could have been you, yes.

Q In fact, we had a telephone conversation in November of 2016; right?

A I believe that could be about the time -- correct time, yes.

Q And you said you were enthusiastic about working with the defendants on this litigation; right?

MR. PENNOCK: Objection.

A I -- I may have said that I am interested in working in this litigation.

BY MS. ALTHOFF:

Q And we told you that we were looking forward to working with you as well; correct?

A I don't remember the exact words, but that could be possible, yes.

Q And you sent us a retainer agreement that you signed saying you'd work with us at a rate of, I think it was -- was it $300 an hour?

A So it was not a retainer agreement. You asked me to send you my fee schedule, and so I sent you my fees. And that was all we agreed upon.

MS. ALTHOFF: Let's show him what's my 36, please.

MR. PENNOCK: Objection.

MS. ALTHOFF: So let's mark this as the next exhibit.

(Whereupon, Exhibit No. 12, Consulting Agreement Between Dr. Gilbert Moeckel and IceMiller Legal Counsel, was marked for identification.)

BY MS. ALTHOFF:

Q Doctor, is this --

THE VIDEOGRAPHER: Twelve.

BY MS. ALTHOFF:

Q Doctor, is this a -- a letter that you sent to my office?

A Yes.

Q Signed by you?

A Yes.

Q And you said, "Pertaining to the requested legal consulting work by IceMiller...in regard to Nexium-induced renal failure, IceMiller agrees to pay Dr. Moeckel the following hourly fees for the rendered legal consulting work."

"Medical chart review with written opinion: $300/hour."

Right?

A Let me quickly read this.

MR. PENNOCK: I'll -- I'll just object. I didn't hear a question.

Go ahead.

A Yeah. So this is a just a legal fee document.

BY MS. ALTHOFF:

Q Okay. That you sent to my office about doing legal consulting with Ice Miller on the Nexium litigation?

A Correct.

Q And following sending this fee schedule to my office, we met in New Haven, did we not?
A As far as I remember, we met before this.
Q Okay. Well, did we meet in January of 2017 at your office for about two hours?
A We met once in my office. I don't remember the exact date.
Q Okay. And we met for about two hours.
MR. PENNOCK: Objection. Not a question.
BY MS. ALTHOFF:
Q Isn't that correct?
A That could be correct.
Q And during that meeting, you told me you were willing to consult with AstraZeneca on this matter?
A I expressed my willingness, yes.
Q And you said that there were some additional materials that you would like to review; is that correct?
A I said I was open to review literature that you would send to me, yes.
Q And did you provide your opinions to me during that meeting with regard to other experts

that we were considering as defense experts?

A I don't remember every detail of that conversation.

Q Do you have any reason to doubt that you and I discussed your opinions regarding other potential PPI kidney experts in this litigation?

MR. PENNOCK: Just note my objection.

Sure he does. You're adversarial counsel.

But go ahead.

A I don't remember that I gave you any suggestions regarding other experts.

BY MS. ALTHOFF:

Q You don't remember one way or the other?

A I -- I don't remember discussing that.

Q Do you recall discussing with me your case report on AIN and omeprazole?

A No, I don't.

Q Do you recall discussing with me your then existing knowledge of the literature on PPIs and kidney injuries?

MR. PENNOCK: Just -- just note my objection. I mean, I -- it sounds like

you're testifying here that these things occurred.

MS. ALTHOFF: I'm asking if he remembers talking about these things with me.

MR. PENNOCK: Well, that -- but there's no foundation. So I'm just going to object this to the foundation.

MS. ALTHOFF: Okay.

MR. PENNOCK: And, therefore -- and the form and --

I mean, if you want to be a witness in the case, that's up to you. But otherwise, I'd like you to rephrase the questions, because your -- your questioning is implying any of this even happened. So --

BY MS. ALTHOFF:

Q Doctor, you do recall meeting with me for about two hours in your office in New Haven, January of 2017; correct?

MR. PENNOCK: Objection to form.

Objection. Asked and answered in several parts.

Go ahead.

A I remember -- I remember meeting with you in my office. I don't remember exactly when.

BY MS. ALTHOFF:

Q Well, did you meet with me before you were retained by the plaintiff's counsel?

A Yes.

Q Was it about a year before?

A That could be approximately right.

Q Did you and I talk about chronic kidney disease and your opinions about chronic kidney disease?

A As I said before, I don't remember much of the details that we talked about.

Q Do you recall whether you discussed with me acute interstitial nephritis and your opinions about acute interstitial nephritis as -- by -- caused by drugs?

A I don't recall any specifics of our conversation.

Q Do you recall discussing the differences between primary and secondary acute interstitial nephritis -- or excuse me -- interstitial nephritis?

MR. PENNOCK: Objection.

A No. I -- I do not recall specifics of

that conversation.
BY MS. ALTHOFF:
Q Do you recall having discussions with me about what you would expect to see if you had a PPI-associated acute interstitial nephritis?
A No.
MR. PENNOCK: Objection.
A As I said, I -- I do not recall details of that meeting.
BY MS. ALTHOFF:
Q Did you, after the meeting, make any notes to yourself about what we discussed?
A No.
Q Do you recall whether I took notes during our meeting about what we discussed?
A I don't recall.
Q And I don't recall this, but did you take any notes during the meeting about what we discussed?
MR. PENNOCK: Objection.
A I -- I don't recall notes taken at that meeting. As far as I remember, it was just a conversation.
BY MS. ALTHOFF:
Q Following the meeting, were you sent

any materials to review?

A I received scientific literature.

Q How much scientific literature?

A A number of articles. I don't recall exactly how many.

Q And what were the -- what was the nature or subject matter of those articles?

A As far as I remember, they pertained to articles on PPI-induced kidney injury.

Q Did that include both chronic kidney disease and acute interstitial nephritis?

A I don't --

MR. PENNOCK: Objection.

A I don't remember for certain.

BY MS. ALTHOFF:

Q Do you still have those binders of materials?

A I do not even know whether I still have them.

Q Did you review the materials in those binders?

A No.

Q When you prepared your materials considered list, did you include any of the materials that had been sent to you by my office?

A No.

MR. PENNOCK: Objection.

A No.

BY MS. ALTHOFF:

Q At any time did you go -- attempt to go find the binders to see whether the same material was already listed on your materials considered list?

A No. I even do not know whether I still have those binders.

Q So between 2017 and 2018, when you were retained by the plaintiffs, did you advise me or anyone at my firm that you were not going to consult with us?

MR. PENNOCK: Objection.

Time frame.

MS. ALTHOFF: I said, "Between 2017 and 2018."

MR. PENNOCK: Right. But you had the meeting in January of 2017, and he's testified he was retained by us in the spring or summer.

BY MS. ALTHOFF:

Q Okay. So between the time of the meeting in January of 2017 and when you were

retained by the plaintiffs in 2018 in the spring or summer, did you advise me or anyone at my firm that you were no longer interested in consulting with us?

A I don't remember doing that.

Q Do you recall at the end of last year, in November of 2020, receiving a reach-out from my office to arrange a follow-up meeting?

A Yes.

Q And my office asked you for some dates?

A Yes. But I declined.

Q Was there any indication in the reach-out e-mail that we had any indication that you were no longer interested in consulting with us?

MR. PENNOCK: Objection. It's a -- calls for speculation.

Go ahead.

A Yeah. As far as I remember, I said in my e-mail that I'm not available.

BY MS. ALTHOFF:

Q Right.

What I'm asking you is: Was there any -- did you take anything from my e-mail to you or my office's e-mail to you that we were no

longer interested in consulting with you?

MR. PENNOCK: Objection to form.

Go ahead.

A Can you please repeat the question?

BY MS. ALTHOFF:

Q Yeah. Let me ask a different question.

So you said you received an e-mail in November of 2020, a reach-out to arrange a follow-up meeting that you declined --

A Yes.

Q -- correct?

A Uh-huh. Yes.

Q Was there any indication to you in that e-mail that my office knew that you were consulting with the plaintiffs or no longer interested in consulting with us?

A No.

Q You could have sent that e-mail at any time prior to November of 2020 post our meeting in January of 2017 if you weren't interested in consulting with us; correct?

MR. PENNOCK: Objection. Argumentative. This is really getting off the rails here.

A No.

BY MS. ALTHOFF:

Q You said you were not available in November of 2020 for consulting with my office. It was because you were already working for the plaintiffs; is that correct?

A Yes.

Q And you were working for the plaintiffs at a rate of $400, instead of $300, which you said you would charge us; correct?

MR. PENNOCK: Note my objection. Argumentative.

Has your rates for all your lawyers, including associates, changed since 2016? 'Cause I'm --

MS. ALTHOFF: You can note your objection for the record.

MR. PENNOCK: -- because --

MS. ALTHOFF: He can answer the question. It's a fully appropriate question.

MR. PENNOCK: Have your rates changed? Have your -- have your rates changed?

MS. ALTHOFF: He can answer the question.

MR. PENNOCK: Their -- their rates have probably gone up more.

A So can you please repeat the question?

BY MS. ALTHOFF:

Q So I had asked you, "You said you were not available in November of 2020 for consulting with my office. It was because you were already working with the plaintiffs; is that correct?"

MR. PENNOCK: Objection.

BY MS. ALTHOFF:

Q And you said, "Yes."

My follow-up question was, "And you were working for the plaintiffs at a rate of $400, instead of $300, which you said you would charge us; correct?"

MR. PENNOCK: Objection.

Objection. Improper use of the prior testimony.

Go ahead.

A So I declined or -- yeah, declined to consult with you because I was already retained by the plaintiff law firm.

BY MS. ALTHOFF:

Q And that happened in 2018 after you had already said you would work with us; correct?

MR. PENNOCK: Objection.

A I have never said that I would work with you.

I sent you the fee list -- the fee schedule, but I never received and I never went into agreement to work with you. In fact, I did not hear from you for another four years or so, until you contacted me in November '20.

So in my opinion, we did not have a relationship at all.

BY MS. ALTHOFF:

Q Despite having met with me on the phone and met with me in your office for about two hours, you didn't consider us having had any type of consulting relationship; is that your testimony?

MR. PENNOCK: Objection to the form.

A That's correct, yes.

MS. ALTHOFF: All right. I don't have anything more for Dr. Moeckel.

(Whereupon, the court reporter requests clarification.)

THE WITNESS: Thank you.

MR. PENNOCK: Okay.

MS. ALTHOFF: All right. Are we coming back -- what time are we tomorrow?

MR. MIZGALA: At 11:00 Eastern. 11:00 Eastern.

COURT REPORTER: Do you want to go off the record?

MR. PENNOCK: It -- it -- yeah. We're going to -- we're going to discontinue for today, and we'll start again at 11:00 tomorrow with Mr. Mizgala.

MR. MIZGALA: Okay.

THE VIDEOGRAPHER: Okay. Off the record 5:18 p.m.

(Thereupon, the deposition was suspended at 5:18 p.m.)

C E R T I F I C A T E

I, Clifford Edwards, Certified Shorthand Reporter, do hereby certify that prior to the commencement of the examination, the witness was duly remotely sworn by me to testify to the truth, the whole truth and nothing but the truth.

I DO FURTHER CERTIFY that the foregoing is a verbatim transcript of the testimony, that said deposition was taken by me stenographically at the time and date hereinbefore set forth, and the foregoing is a true and accurate transcript of the testimony.

I FURTHER CERTIFY that I am neither of counsel nor attorney to any of the parties to said suit, nor am I an employee of any party to said suit, nor of any counsel in said suit, nor am I interested in the outcome of said cause.

Witness my hand and seal as Notary Public this 12th day of July, 2021.

Clifford Edwards

Notary Public

My commission expires: 9/30/2021

J U R A T

I have read the foregoing 217 pages and hereby acknowledge the same to be a true and correct record of the testimony.

_____

Gilbert W. Moeckel, M.D., Ph.D., FASN

Subscribed and sworn to

_____.

Before me this _____ day of _____,

2021.

_____

Notary Public

My Commission Expires:

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